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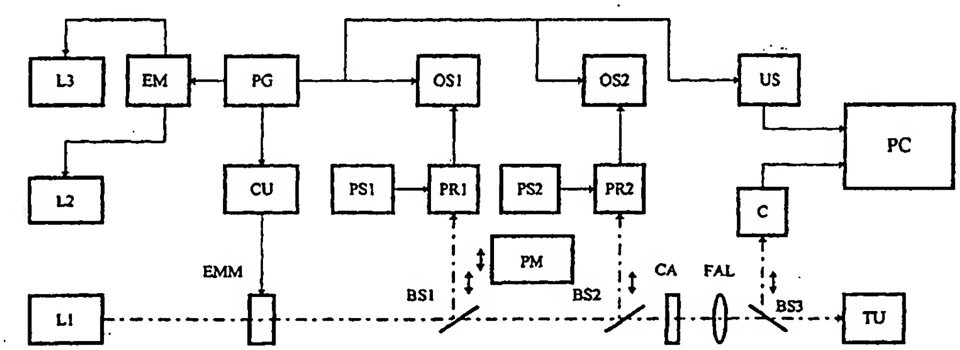
(54) Title: METHOD AND SYSTEM FOR LASER TISSUE WELDING



L1 – laser (λ=0.63 μm); L2 – laser (λ=0.68 μm); L3 – laser (λ_1=0.53 μm, λ_2=1.06 μm); EMM – electro-mechanical modulator; CU – control unit; PG – pulse generator; EM – electronic modulator; BS1, BS2, BS3 – beam splitters; PR1, PR2 – photo-electronic amplifier; PS1, PS2 – power supply unit; OS1, OS2 – oscilloscope; CA – controlled aperture; FAL – free aberration lens; TU – technological unit; C – CCD camera; US – synchronization unit; PC – computer; PM – power measuring device.

(57) Abstract: A method and system (5a) for joining adjacent tissue portions using lasers, the method including the formation of a plurality of non-contiguous laser formed elements along a weld line, the elements being positioned in a predetermined pattern with respect to each other and each having a predetermined cross-sectional configuration. The elements can be independently created in order to achieve a desired absolute and relative extent of denaturation, coagulation, and/or carbonization within the tissue, and particularly within the individual elements. In use, energy from a laser source can be applied to an accessible surface of the contacted tissues in manner that provides an optimal combination of a) the number and relative pattern of elements along a weld line; b) the cross-sectional of the individual elements along the weld line; and c) tissue impact within and surrounding each element (e.g., in terms of the absolute and/or relative extent of denaturation, coagulation, and/or carbonization within each element). The method and system (5a) can include a diagnostic component that permits the operator to obtain a substantially real-time assessment of various parameters, in order to permit an optimal weld to be achieved.

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METHOD AND SYSTEM FOR LASER TISSUE WELDING

CROSS REFERENCE TO RELATED APPLICATIONS

The present application is a continuation of US patent application filed August 20, 1999 and assigned Serial No. 60/150,070, the entire disclosure of which is incorporated herein by reference.

TECHNICAL FIELD

The present invention relates to methods and systems for joining tissue portions. In particular, the invention relates to methods and systems for joining tissues by the use of lasers, as in laser tissue welding.

BACKGROUND OF THE INVENTION

The surgical suture is presently the most common means used for connecting adjacent or overlapping portions of biological tissue. Suturing provides a reasonably flexible technology, that can be adapted almost for any conditions arising in tissue. This technology is relatively inexpensive, reliable and accessible. Nevertheless, the use of sutures can result in tissue damage, particularly when the needle is passed through tissue and the knots are initialized. Moreover, since the suturing material is foreign to the organism, the use of sutures can lead to inflammation, as well as granuloma, scars and stenoses. Moreover, it is recognized that sutures do not give tight connection of tissue, and the overall success of the procedure can be dependent on the surgeon's individual practices and skills.

Connecting tissue with brackets and clips can provide more stable and secure results, since the force of tissue compression is determined by the seaming device. As compared to handmade sutures, the use of brackets and clips has some restrictions as well, particularly in terms of the thickness and integrity of tissue. A further advantage of brackets and clip is their usefulness with endoscopes and laparoscopes. Several of

the defects associated with sutures apply to brackets and clips as well, however, including the relatively large force needed to tighten the brackets, and the corresponding technical limitations that exist on the minimum size of such suturing devices.

In recent years the use of laser beam tissue "welding" has been applied as well, involving the application of laser energy for tissue connection. Upon delivery of the laser beam to overlapping tissue, the molecular structure of tissue is changed, creating attachment between modified tissue molecules and their neighbors. An early study of Shober et al. (7) demonstrated loosening of the collagen triple helix and corresponding interactions between collagen strands, and concluded that collagen "bonding" was responsible for laser welding. Under optimum conditions laser beam welding can be conveniently applied to produce solid connection of tissue with less trauma than other known methods.

Various laser techniques for joining tissue have been developed and improved to the point where they are now already in common usage, and are expected to find considerably greater applications and use over the course of the next decades. See, for instance, L. Bass and M. Treat, "Laser Tissue Welding: A Comprehensive Review of Current and Future Clinical Applications", in *Lasers in Surgery and Medicine* 17:315-349 (1995), the disclosure of which is incorporated herein by reference. These developments have involved studies of the underlying mechanisms of laser welding, as well as the development of related methods and materials (e.g., the lasers themselves, solders, and the like).

As described in Bass, et al., however, "there are still major gaps in our understanding of the actual mechanism involved [in laser welding]". Table 1 of Bass et al. shows data describing distinctive attributes of the types of lasers most commonly used in experimental investigations. Yakimenko et al. (20) discuss the effects of various laser welding modes on the walls of blood vessels. Several studies have attempted to develop a model of vessel tissue coagulation, taking into account optical and thermodynamic tissue properties. Investigations of anastomoses firmness have shown that such factors as tissue thickness, optical properties and the humidity of vessel walls can affect the choice of radiation used. For example, for walls thickness of 0.3 mm, it was found optimal to use a laser having a wavelength of 1 μm

to 1.4μm, average radiation power 5 W to 30 W, beam diameter 0.1 mm to 0.3 mm and exposure time 0.05 s to 0.2 s (20).

A comprehensive review of clinical applications of laser tissue welding is presented in Bass et al. (12). Based on the analysis of published experimental work, it is possible to determine several areas of experimental research in laser tissue welding. The first area involves the choice of laser characteristics, and in turn, their modes of operation with various organs or tissues, in an attempt to reveal optimal parameters and principles. Several studies have investigated optical and thermal tissue characteristics that might be useful in applying and controlling the process of welding. Most of the researchers used IR- sensors, enabling them to monitor temperature on a surface, as well as the radiation power and exposure time (25-28). Such approaches tend to be quite subjective, however, since the longitudinal gradients of temperatures can strongly depend on a particular tissue, including its thickness and degree of compression.

Another area of research involves the choice of appropriate biological solder, which can be used to locate and/or intensify absorption of radiation of a given wavelength, and in turn, to effectively control the distribution of radiated energy in tissue volume (29-31).

In addition to clinical and experimental descriptions of laser welding, a number of theoretical studies have been conducted as well. The variety of optical and thermophysical properties of tissue is rather wide, particularly since a large variety of lasers with wide wavelength range are accessible to the surgeons. Furthermore, wide variations can exist in the many parameters of laser radiation – including power capacity, pulse rate, time of exposure and other. Moreover, the art has not yet determined a complete understanding of the mechanism of laser tissue welding. In turn, theoretical studies, and particularly computer modeling of physical and chemical processes that may occur upon the interaction of laser radiation with tissue, are lacking.

On a related subject, only a handful of issued US patents appear to mention the possibility of delivering the laser energy in the form of what might be considered patterns of some sort. For instance, US Patent No. 5,281,211 (Parel, et al., "Noncontact Laser Microsurgical Apparatus") describes a noncontact laser

microsurgical apparatus and method for marking a cornea of a patient's or donor's eye in transplanting surgery or keratoplasty, and in incising or excising the corneal tissue in keratotomy, and for tissue welding and for thermokeratoplasty. In one embodiment, an adjustable mask pattern is inserted in the optical path of the laser source to selectively block certain portions of the laser beams to thereby impinge only selected areas of the cornea. By careful selection of the laser generating means the corneal tissue may be heated only sufficiently to cause shrinkage of the tissue in selected areas to alleviate astigmatism and/or corneal refractive error.

See also, US Patent No. 5,092,864 (Hayes, et al., Method and Apparatus for Improved Laser Surgery"), which describes a method and apparatus for providing more precise placement and control of the delivery of laser energy. The apparatus includes a pulse-controlled dye delivery system which may be coordinated with the delivery of laser energy to predetermined tissue. The pulse-controlled dye delivery system includes an ejection head capable of ejecting drops of liquid dye with the diameter of each drop being less than two hundred microns. The dye is responsive to the wavelength of energy delivered by the laser performing the surgery to convert the laser energy from the surgical laser to tissue thermal energy.

The effects of laser beams on a living body will depend on numerous factors, for example, wavelength, energy or power intensity, and difference of waveform such as continuous wave or pulsative wave. The effects of a laser beam can be classified into four regions, namely, the photochemical, thermal, photoablative and electro-mechanical regions. The thermal region is used as a laser scalpel. See, for instance, US Patent No. 5,407,443 (Kobayashi, et al.) which describes a laser operation device for insertion into a region to be irradiated and which is optimally used as an intraocular device to treat cataracts, glaucoma or the like.

Kobayashi et al. describe the manner in which the temperature of tissue irradiated by a laser is elevated because of a rapid increase of molecular temperature. Since the depth reached by the energy of the laser beam or the temperature of the tissue attained is determined by the combination of wavelength, irradiation time and irradiation area of the laser beam, control is possible including the suppression of cell activity, as well as melting, coagulation, carbonization, and evaporation of proteins. Further, the Kobayashi et al. patent suggests that a laser having a wavelength

coincident with an absorption peak of water (which is a main constituent ingredient of the living tissue) can be used at a high peak power and at an ultra-short pulse width, so that the living tissues can be incised scarcely undergoing thermal damages.

See also, United States Patent 5,071,417 (Sinofsky), which describes an apparatus and methods for laser fusion of biological structures, using a laser for delivery of a beam of radiation to an anastomotic site, together with a reflectance sensor for measuring light reflected from the site and a controller for monitoring changes in the reflectance of the light of the site and controlling the laser in response to the reflectance changes. In its background section, this patent describes the manner in which argon and other visible light lasers tend to produce less than satisfactory effects. The output of argon lasers and the like was found to be heavily absorbed by blood and subject to substantial scattering within the tissue These effects combined to create a narrow therapeutic "window" between a proper amount of energy necessary for laser fusion and that which induces tissue carbonization, particularly in pigmented tissues and tissues that have a high degree of vascularization. The patent remarks that the development of new solid state laser sources have made prospects brighter for efficient, compact laser fusion systems suitable for clinical use. Such systems typically employ rare, earth-doped yttrium aluminum garnet (YAG) or yttrium lithium fluoride (YLF) or yttrium-scadium-golilinium-garnet (YSGG) lasers. This patent refers, in turn, to U.S. Pat. Nos. 4,672,969 and 4,854,320, both issued to Dew, disclosing the use of a neodymium-doped YAG laser to induce laser fusion of biological materials and to obtain deeper tissue penetration. The Dew patents disclose the use of computer look-up tables to control the dose based on empirical data. Unfortunately, the patent recognizes that absorptive properties of biological structures differ considerably from one tissue type to another, as well as from individual to individual, making dosage look-up tables often unreliable. The Sinofsky patent is said to address a need for better laser fusion systems that can accurately control the formation of an anastomotic bond to avoid thermal damage and achieve optimal results.

When tissue is exposed to high-energy radiation (e.g., having a power density of greater than about 1 W/cm^2) a thermal effect occurs. As radiation power density increases the tissue becomes hotter. When heated, the configuration of many types of

macromolecules is changed (6), which, together with dehydration, results in varying effects on the viscosity, density, thermal and optical properties of tissue. At an initial level of heating, tissue begins to dehydrate and becomes coagulated, after which it is thermolized and carbonized (2, 3). The average power radiation density values for achieving these processes are, approximately 10 W/cm^2 to 50 W/cm^2 for dehydration and coagulation, 50 W/cm^2 to 1000 W/cm^2 for thermolysis and carbonization start-up (4). Complete carbonization is reached at temperatures about 200 °C to 220°C, and that the carbonized framework burns up at 400°C to 450°C.

Electron microscope investigations have shown that heating tissue to a temperature above 60°C leads to erosion of the threefold protein spirals. The bonds and/or attractive forces between complex spiral molecules of protein are compromised, whereupon the spirals are transformed in a nonspecific fashion into fibrous structures having strong links between the fibers. A number of the researchers assume that these links are responsible for the tissue welding phenomenon (11).

The temperature at which protein denaturation occurs lays in the range 60-80°C (12). Certain objective criteria of the effectiveness of thermal tissue welding include: the firmness of the tissue connection, the duration of the welded suture (e.g., as compared to tissue healing kinetics), and the area of tissue affected (e.g., the size of a zone where tissue dies away under thermal influence). In turn, numerous experiments have shown that the quality of welding depends on radiation features (e.g., wavelength, power, distance, spectral characteristic of radiation source), the exposure time, and properties of the tissue itself.

Tissue can be considered as a flat layer with constant thermophysical properties (32). The structure of volumetric absorption of radiation can be determined on the intensity of dropping radiation and the reduction factors in a tissue accounting absorption and unitary dispersion. The heat conductivity for a received three-dimensional axis-symmetrical problem was solved analytically by decomposition on Besets functions. Various types of lasers were analyzed, including a $C0_2$-laser (wavelengths 10.6 μm), an argon laser (0.5-0.6 μm), its depth of penetration of a beam being essentially larger, than for a $C0_2$-laser, but its radiation being strongly absorbed by hemoglobin), and a Nd-YAG laser (wavelength 1.06 μm, it's absorption being 4-5 time less than that for a argon laser, thus providing the ability to achieve

tissue warming up with a narrow beam penetrating up to several mm in the depth). The authors evaluate experimental data up to the temperature 75°C. At temperatures above 58°C coagulation begins, while the processes of evaporation (at temperatures above 100°C), carbonization and burning out of carbonized sites at further increase of temperature were not considered (32).

In a numerical model of irradiated tissue, proposed in Cummins, et al. (33), the tissue is also considered as an axis-symmetrical flat layer. The values of thermophysic parameters of a tissue were varied according to the non-uniformity of its structure and with regard to coagulation, evaporation and carbonization. A three dimensional, axis-symmetrical calculation of thermal fields in tissue is considered in Zweig et al. (34), using a $C0_2$ laser. The evaporation of water contained in tissue and heat and mass exchange were considered in a biphase environment.

In the review by Welch (13) several mathematical models for the processes of interaction of laser radiation with tissue are discussed. Factors such as the non-uniformity of thermophysical properties and multilayerness of tissue are considered, together with evaporation (and, accordingly, the changes of water content in tissue). The various thermophysic parameters of tissue during heating are considered as well as heat absorption while protein is denatured. External soft tissues, such as the eye and the skin were considered basically, since the main purpose of research was formulation of generalized criterion of safety (from a point of view of an allowable degree of scalds). The author remarks that various mathematical models take into account the dispersion of radiation in a tissue, temperature dependence of tissue thermophysic parameters, evaporation of water, the change of thermophysic parameters with water evaporation and the change of absorption factors during coagulation. At the same time, within the framework of one model all these parameters are not simultaneously taken into account.

In Ogirko et al. (35) a mathematical model for the description of physical-mechanical and chemical processes, occurring in tissue under laser radiation influence is offered. The tissue was simulated as a composite environment. The structure of a tissue has been assumed as biphase (firm body - liquid), consisting of reacting chemical components. An approach concerning the mechanics of continuous environment and thermodynamics of irreversible processes is applied. The model is

based on a hypothesis of local balance. The system of nonlinear differential equations in partial derivatives has been solved using a finite-difference method. A gear of optimal control of laser beam is proposed. It should be noted, that the main purpose of the researchers is the modeling of a laser scalpel operation.

In contrast to their use in tissue welding, lasers are also commonly used for ablating, rather than joining, tissues. See for instance, Wojcik, et al., US Patent No. 5,860,968 ("Laser scanning method and apparatus"), which describes the manner in which carbon dioxide laser beam has been used for many years in the ablation of living tissue. The laser causes a temperature rise in the tissue primarily due to the absorption of laser radiation by water in the tissue. When this water is heated to its boiling point, it causes an explosive ablation of the surrounding tissue. However, heat transfer to adjacent tissue may cause thermal damage, resulting in tissue necrosis, desiccation, or carbonization ("char") that hinders further ablation until the "charred" tissue is removed. One technique the patent mentions to minimize damaging heat transfer to adjacent, unablated tissue is to cause a rapid temperate rise in irradiated tissue, e.g., by the use of a "superpulse" operation. The Wojcik patent also refers to the ability to maintain a small spot size and close distance to the target tissue and rapidly move the small beam of laser energy over the target area, and concludes that a great deal of manual dexterity and experience is required to accomplish uniform ablation over a large area by hand. One proposed mechanical method for doing so is disclosed in U.S. Pat. No. 5,411,502 issued to Zair on May 2, 1995, which is directed to a system using one or two electromechanically rotated mirrors in combination with a focusing lens to cause the laser beam to trace Lissajous figures. The drawbacks to this system are said to include the cumbersome and complex mechanical components and the effort required to maintain the mirrors and focusing lens in precise alignment.

The Wojcik patent itself addresses the various shortcomings it sees in the art by providing a laser scanning method and apparatus to uniformly deliver the beam of laser energy to a target site. The method for involves uniformly moving the beam of laser energy in a predetermined pattern over the target site. In one form of the invention, the beam is moved by manipulating conduit through which the beam travels, with the proximal end of the conduit being held in fixed alignment with the laser energy source and the distal end of the conduit being moved in a predetermined

pattern. The laser energy source is pulsed at a predetermined power level and for a predetermined frequency and duration, and the conduit is moved at a predetermined speed in coordination with the pulses of laser energy to uniformly scan the laser beam over the target area and achieve uniform tissue ablation in the target area. In turn, the laser delivery system is said to include a generator of laser energy, a guide for conducting the laser energy to a target site; and a device for scanning the laser energy at the target site, the scanning device comprising a conduit for conducting laser energy; and a device for moving the conduit in a predetermined pattern to uniformly scan the target site with laser energy and achieve a uniform and thorough ablation of the target tissue at the target site. In another aspect, the laser generator is configured to generate pulses of laser energy of a predetermined power, frequency and period or duration, and the moving device is configured to move the distal end of the conduit at a predetermined continuous speed in coordination with the frequency and duration of the laser energy pulses so that the laser energy is delivered uniformly to the target site.

In spite of the considerable progress made to date, the technique of tissue welding remains in its relative infancy. To move beyond this point will require an improved understanding of the mechanisms involved, and in turn, the development of innovative materials and methods for improving and optimizing those mechanisms.

BRIEF DESCRIPTION OF THE DRAWING

In the Drawing:

Figures 1a and 1b show alternative cross-sectional schematic views of laser formed elements for use in the present invention.

Figure 2a shows a variety of different laser point elements in side elevation and cross section according to the present invention, while Figure 2b shows a variety of geometrical combinations (i.e., patterns) of laser point elements according to the present invention.

Figure 3 shows a chart of the spectral dependencies of transmission coefficients.

Figure 4 shows a schematic view of a system of a multispectral laser welding system.

Figure 5 shows schematic views 5a, 5b and 5c of a laser welding system for use in the present invention.

Figure 6 shows a chart of the spectral characteristics of quartz plates.

Figure 7 shows an optical scheme of an MPS-2000 spectrophotometer.

Figure 8 shows an optical scheme of a U-3400 spectrophotometer.

Figure 9 shows an optical scheme of a multitarget unity RTA-2000.

Figure 10 shows an optical scheme of an IR-435 spectrophotometer.

Figure 11 shows a chart of the reflection, transmission and absorption indicies of two-layer tissue samples.

Figure 12 shows a chart of the absorption index of compressed tissue.

Figure 13 shows a chart of the spectral characteristics of tissues in the IR-range radiation.

Figure 14 shows a chart of the results of calculations for unfocused laser beams.

Figure 15 shows a chart of the results of calculations for focused laser beams.

Figure 16 shows a chart of the characteristic laser beam power distribution curve.

Figures 17 through 21 show various microphotographs of the effects of laser radiation on tissue.

Figure 22 shows a schematic view of a system of this invention.

SUMMARY OF THE INVENTION

The present invention provides a method and system for joining adjacent tissue portions using lasers, the method comprising the steps of forming a plurality of non-contiguous laser formed elements along a weld line, the elements being positioned in a predetermined pattern with respect to each other and each having a predetermined cross-sectional configuration. In a preferred embodiment, the elements are independently created in order to achieve a desired absolute and relative extent of denaturation, coagulation, and/or carbonization within the tissue, and particularly within the individual elements themselves. As described and used herein, the effect of laser energy on tissue, e.g., under conditions of increasing laser energy and/or exposure time, will be considered to involve the following steps, in approximate order

of occurrence (and corresponding with increasing tissue temperatures): protein denaturation, dehydration, coagulation, thermolysis, and carbonization. In turn, the net effect on tissue can be assessed by determining the absolute and/or relative extent of denaturation, coagulation, and carbonization, since dehydration and thermolysis are more akin to the processes involved, as compared to the detectable result achieved.

In a preferred embodiment, therefore, the method comprises the steps of

1) contacting two or more tissue portions, in a manner that provides respective surfaces of the tissues in direct or indirect contact with each other, such that the contacted tissue portions provide at least one surface accessible to a source of laser energy;

2) providing a source of laser energy; and

3) applying energy from the laser source to the accessible surface of the contacted tissues in manner that provides an optimal combination of;

a) the number and relative pattern of elements along a weld line;

b) the cross-sectional structure of the individual elements along the weld line; and

c) tissue impact within and surrounding each element (e.g., in terms of the absolute and/or relative extent of denaturation, coagulation, and/or carbonization within each element and/or surrounding tissue).

The tissue portions can be directly or indirectly "contacted" in any suitable manner, e.g., they can be provided in a directly overlapping or abutting relationship with respect to each other and/or they can be indirectly contacted by the use of a secondary material, e.g., an intermediate or surrounding layer of an exogenous treated natural tissue, for instance, that is itself susceptible to laser radiation in order to form an integral bond with tissue portions to be welded.

In one preferred embodiment, the predetermined weld line pattern is a primary pattern selected from the group consisting of straight lines, zigzag, wave forms, and the like, examples of which are shown in Figure 2b. In a related embodiment, the pattern can include one or more secondary patterns (also shown in Figure 2b, e.g., with adjacent, grouped elements in the form of small geometric patterns), the groupings themselves preferably being formed in predetermined positions along a weld line. As used herein, the term "primary pattern" will refer to the position of a

element within a weld line, e.g., along a point forming the overall weld between two tissue portions, while the term "secondary pattern" will refer to the position of a element within a subgroup of adjacent elements, e.g., to form a secondary structure or geometric pattern that covers a larger area than any single element, but a smaller area than the weld line itself. The primary and secondary patterns can be provided in any suitable manner, e.g., by the use of pattern-imposing masks, pattern positioned solder, and/or in a controlled manner by controlling the location and other relevant parameters of the laser head itself.

In order to create a pattern, an apparatus for use in the present system preferably includes a hand-held or automated instrument, e.g., a pen-like device adapted to be held by the surgeon in the course of applying the laser energy. The tip of the "pen" delivers the laser energy (impulse) to the tissue, and can be used to create either a single point (element) or patterns of such points in the sutured tissue. The tip of such a device can be permanent or changeable, e.g., by physically changing the tip itself or by altering computerized instructions thereto, in order to create different point patterns. Laser tips of this invention can also have a pre-defined point pattern such as an arc, triangle, a plurality of points in a row, or a single point. The surgeon can use the impulse delivery device in a variable and controllable mode and/or can lock the device in one or more fixed positions in order to move it around the tissue.

In a further preferred embodiment, the cross-sectional configuration of the elements, examples of which are shown in Figure 2a, is independently selected from the group consisting of elements of a generally cylindrical, multilateral, pyramidal, conical or egg shaped configuration. The elements can be either solid through their entireties, or the form of cavities within (partially or wholly through) the tissue. In yet a further preferred embodiment, the elements can independently extend partially or fully through one or both portions of adjacent tissue (and/or into or through intermediate layers as described herein). In one preferred embodiment, for instance, the elements are formed substantially at or near the interface between two tissue portions, so as to minimize the impact and possible trauma to surrounding tissue.

Tissue impact can be controlled and coordinated between individual elements, so as to provide an optimal extent and balance of denaturation, coagulation and/or carbonization. Tissue heating to the temperature above 60°C, for instance, typically

leads to erosion of the threefold protein spiral. In denaturation, the links between complex spiral molecules of protein are altered, transforming the spirals into a fibrous structure having strong links between the newly formed fibers.

The method and apparatus of the present invention can be applied to a variety of laser welding approaches. Such parameters as power level and exposure time can be selected to obtain suitable element structures, e.g., resembling a "hollow clinch", in the form of a substantially hollow element. In one embodiment, as seen in Figure 1a, the method of forming a weld of this invention can involve the use of laser energy to form one or more hollow elements each surrounded by a zone of denaturated protein. Given their numbers and relative positions along the weld line, the elements can collectively provide a suture weld line having the desired toughness and stability, and without the need to provide carbonized tissue.

An alternative embodiment, shown in Figure 1b, involves the laser formation of one or more carbonic elements between the tissue portions. Particularly when there is no gap between the sutured tissue pieces, a substantially cylindrical coagulated zone can be provided that surrounds the carbonized framework, providing suture firmness that can be even higher that of the first embodiment above. Moreover, the element can be formed at substantially the interface between the tissue portions, rather than through the whole depth of the portions, thereby further reducing trauma .

Those skilled in the art, given the present description, will appreciate the manner in which the delivery of laser energy can be controlled to achieve the results described herein. The optical properties of tissue samples can be quite different, even within different portions of the same organ, e.g., in terms of temperature at the zone of protein denaturation, the degree of compression of welded tissue samples, and the like. Generally speaking, however, the denaturation reaction proceeds slowly at tissue temperatures below about 60°C and increases significantly as temperatures exceed about 70°C. For instance, using calculations based on the Arrenius equation, it can be determined that at 60°C the speed of reaction equals 5 s^{-1}, at 70°C - $5.5x10^3$ s^{-1} and at 80°C - $4x10^6 s^{-1}$. In turn, the combination of short exposure times with high power density will typically be less preferred, since to obtain firm connection of tissue portions the denaturation process should generally be completely terminated in a rather large zone. The temperature of the reaction is therefore preferably uniform in

the whole volume under the zone surface and enough high to intensify the denaturation process.

The present invention also provides the ability to control the extent and type of tissue impact within and/or surrounding individual elements, and in a preferred embodiment to diagnose such impact in the course of the procedure itself, so as to permit further control options. For instance, the method can be used to provide elements having an optimal combination of zones of tissue (or components of the tissue) that has been denatured, coagulated, and/or carbonized. In one preferred embodiment, for instance, an element is provided in a manner that has a cavity in the form of a substantially hollow core, surrounded by a substantially concentric zone of carbonized tissue, which itself is surrounded by a ring of coagulated tissue and then a ring of denatured tissue, or more preferably which is surrounded by substantially denatured tissue.

As used herein, the word "denatured" and inflections thereof, will refer to tissue in which the tertiary structural characteristics of its proteins are detectably altered, while the word "coagulated" and inflections thereof will refer to the conversion of the tissue or its components (e.g., cells or cellular structures) into a solid, semi-solid or gel-like mass. Under the conditions of the present invention the area of coagulated tissue is preferably minimized, since it tends to provide the least preferred combination of low strength and scarring. Given the present description those skilled in the art will appreciate the manner in which laser energy can be applied to tissue in order to various combinations (including absolute and relative extents) of denatured, coagulated, and carbonized tissue. Applicants have found that carbonized tissue is preferred in that it tends to provide a secure initial lock, while is also conducive to being removed by the body over time with little or no scarring or undue trauma. Finally, the word "interface" as used herein will refer to the physical contact point or points between tissue portions (including natural tissues and/or intermediate layers as described herein), and in turn, to the zone of laser energy deposited at or near the interface in order to effect a bond between the two portions.

The present invention provides a method and related apparatus for laser tissue welding. The method and apparatus of the invention can be used to optimize welding modes and to provide advanced equipment design. A preferred system of this

invention comprises one or more components selected from the group consisting of a laser radiation source; a radiation transport component; one or more welding clamps; a cooling component with optics and sensor protection; a diagnostic component system; and an automatic welding control. Such a system can include, for instance:

(1) Source of Radiation:

In a particularly preferred embodiment, the radiation source includes one or more lasers or set of lasers;

(2) Radiation Transport Component:

The apparatus preferably further includes a radiation transport component, e.g., in the form of a set of fiberoptics cables, electrical and micro optical components adapted to transport radiation from laser to tissue;

(3) Welding Clamps:

The system can further include one or more welding clamps, e.g., with sensors, which function to hold welding tissue together and transmit information about the welding process;

(4) Cooling Component:

In a preferred embodiment, the system of this invention also includes a cooling device adapted to cool optical components, sensors and tissue surfaces; absorb extra radiation from tissue; remove tissue particles, vapors or eliminate mists formed during welding process; and protect sensors from tissue particles.

(5) Diagnostic/monitoring Component:

The apparatus preferably also includes a set of sensors, cameras and electrical components adapted to diagnose various parameters within the tissue before, during and after laser welding process;

(6) Automatic Welding Control:

As a further preferred component, the present system further includes a computer and monitor adapted to receive and compile information; provide substantially real time information for surgeon about tissue welding process, and permit control thereof.

Given the present description, those skilled in the appropriate art will be able to determine the manner in which the above components (e.g., particularly components 2, 3, 4 and 6) can be custom designed for particular applications

Although various parts of the system or its components may be known in the art, the system as a whole is considered novel, as are several of its components. The laser tissue welding system of this invention will permit the operator to perform a wide variety of surgical operations in various fields of surgery. Laser delivery tips, for instance, can be changeable to accommodate different types of surgical (including laser tissue welding) operations as well as tissue diagnosis.

DETAILED DESCRIPTION

The present invention addresses a variety of present concerns, including: (1) the ability to irradiate tissue with laser energy in order to obtain a surgical suture with specified features; (2) the development of related equipment and circuitry for laser welding in order to achieve such specified features in various types of tissue; and (3) the development of computer software for controlling the apparatus in order to achieve the desired features, and for use in modeling of the physical-chemical processes occurring in tissues influenced by powerful laser radiation.

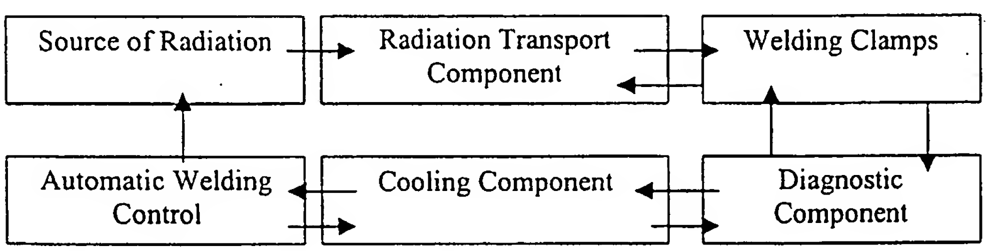
Applicants have, in turn created a system that permits the user to: (1) create a laboratory testing ground for the development and substantiation of a method of laser tissue suturing; (2) review the optical properties of tissue, including particular features of laser radiation of various spectral ranges and it's interaction with various kinds of tissue and resultant tissue properties; (3) improve control methods for maintaining laser beam parameters while investigating the influence of radiation on tissue; (4) analyze and compare various experimental tissue laser suturing processes; (6) optimize parameters of laser radiation (e.g., including spectral range. duration, pulse ratio, power capacity of laser pulse); (7) investigate and determine the firmness of a laser welded suture and it's optical properties; (8) develop a three-dimensional axis-symmetrical non-stationary model of the processes of tissue interaction with laser radiation; (9) accomplish optional accounts for specified tissue types and definition of optimum radiation source parameters; and (10) compare the calculated results with experimental data and updating the model.

Using thin intestine tissue as a model, Applicants have shown that it is possible to develop at least two basic approaches for tissue connection. One is based on dot influence of powerful radiation on tissue pieces being sutured. Power level

and exposure time are selected to obtain a structure resembling a partially or entirely hollow cavity (Fig. 1a) surrounded by a zone or layer of coagulation.

A second, and more preferred, approach for forming welds of this invention involves the formation under the influence of radiation a carbonic joint-element between the tissue pieces (Fig. 1b). If there is no gap between the sutured tissue pieces and a coagulated cylindrical layer is surrounding the carbonized framework the firmness of the suture may be even higher that of the former option. Moreover, the joint point can be formed not on the whole depth of sutured pieces but placed only near the border between them, thereby leading to a reduction of traumatic effect.

Applicants have developed a system that includes prototype equipment for laser tissue welding according to the method of this invention. In a preferred embodiment, the system permits the user to optimize the welding modes and to improve constructional decisions. A prototype system of this invention is shown in the block diagram below. This diagram represents experimental prototype, which has been used in experiments. Advanced prototype (production prototype) can have a different layout, with a corresponding block diagram dependent on the configuration of the advanced prototype, e.g., with some of the various modules being combined. The production prototype schematic can be represent as a following diagram:



The prototype assembly consists of a set of lasers with selective radiation in the wavelength range of about 0.5 microns to about 1.3 microns. A set of lasers with re-tunable wavelength may be used instead. A unit for transportation of laser radiation is represented by a set of fiber-optics cooled with water (particularly since the required power is expected to exceed 0.53 W/cm^2).

As can be seen in the schematic of Figure 22, a main element of the prototype shown in the above diagram is an endoscopic device, which includes some or all of the following components:

1) a laser beam focusing unit,

2) a tightening unit to hold tissue pieces in contact, and optionally to compress the tissue pieces in the course of laser welding,

3) a temperature control for monitoring and controlling the tissue surface temperature,

4) a surface structure control for monitoring the surface structure of the welded tissue sample (e.g., a polarizing device to measure refraction and absorption indices of the welded tissue surface)

5) depth control for monitoring and controlling the tissue burn-through with laser radiation,

6) a firmness control for determining the firmness of welded suture,

7) a visualization system, including a CCD TV camera, and

8) a specialized PC to control the operation modes of equipment and to process the results, including obtained images of the welded tissue.

The method and system of the present invention can be used to provide an optimal combination of tissue weld strength with reduced trauma. Without intending to be bound by theory, it would appear that this combination occurs, in part, by virtue of the ability to press the tissue portions together in order to force blood from the weld site and increase the density thereof. In turn, the transfer of radiation between pieces can be increase by about an order of magnitude, so that the amount of heat discharged on the upper layers will be significantly less than the amount discharged at the interface between the pieces. This approach also permits the user to focus a laser beam on this border (e.g., by means of a focal cross-over), thereby increasing the effective heat discharge.

In a preferred mode, the radial temperature gradients beyond the scope of the beam aperture are as great as possible, thereby ensuring that the thermal action of radiation is maintained locally and with lesser chance to influence the surrounding tissue. This can be balanced with the desire to maintain a zone of denatured protein that is typically as large as possible, to establish necessary firmness of a suture. The

system of this invention permits an optimal balance to be established between the exposure time, focal point and beam size, in order to achieve an desired and optimal balance between the size of the thermal destruction zone and the firmness and stability of the individual weld elements, and in turn, the overall weld line.

A mathematical model of the temperature field in the course of laser irradiation of tissue, as described herein, can be performed using any suitable software language, e.g., FORTRAN. The software can have the following structure:

1. A module for initial data input, including initial conditions of the tissue itself, including thermophysical parameters of the tissue portions, as well as relevant aspects of the laser apparatus, including laser power capacity and/or pulse power, mode of radiation, various relevant constant parameters, laser focusing parameters, and the like.

2. A control module in which initial conditions are stated, and information is received from the program application, which are together processed to solve a system of ordinary differential equations. The modes of system integration can be corrected at this time, and improvements can be made to the laser tissue irradiation modes. This module is the main software for the integration of a system of ordinary differential equations.

3. A standard program is provided for the integration of rigid systems of ordinary differential equations, incorporating an algorithm for the simulation of absorption and scattering.

4. A subroutine can be included for calculating nonstationary heat transfer equations under conditions of axial symmetry and in a specified impulse, involving the processes of heating the tissue water component and the formation of various zones or cavities in the tissue portions. This subroutine can be called up by a program for integrating a system of ordinary differential equations over time.

5. One or more subroutines for calculating various thermophysical parameters of the tissue, and specific heat extraction, basedon time and the temperature of a tissue fragment. These subroutines can be used by the program to calculate various values for the nonstationary heat transfer equation described above.

6. Subroutine to address danger degrees of radiation. Along these lines, the software can also provide the ability to visualize the temperature field on a real

time scale, with calculations being relayed to form a colored image of the temperature field within the tissue on a monitor screen. This feature permits the operator to view the dynamics of the process directly, and as the calculations are made.

7. The calculations of specific heat extraction from the radiated tissue can be executed by a separate program or subroutine, with a technique for the simulation of absorption and scattering at various radiuses of an aperture in the radiated tissue fragment, and can be averaged to account for discrete elements.

EXAMPLE 1

Experimental research of laser tissue welding.

A multispectral experimental unit was created having characteristics close to the published scientific literature, in order to approximate many of the lasers most widely used in medical practice (12), including gas lasers, such as $C0_2$ (λ =10.6 µm) and argon lasers (λ =0.51 µm, 0.49 µm), neodim lasers (λ =2.94 µm, 2.06 µm, 1.32 µm, 1.06 µm, 0.53 µm), and semi-conductor lasers (λ =0.81 µm).

The efficiency of a particular laser application for tissue welding can be determined by evaluating the efficiency of energy delivery to the tissue parts being welded. It is preferable to provide uniform energy distribution at the weld point, and in particular, at the interface between tissue portions. This can be achieved by control of the laser radiation power (energy) delivered to the welding zone, as well as on time-spatial distribution. The influence of laser radiation spectral-power features on the efficiency of welding has been analyzed in some published papers, but it appears that Applicants are the first to have considered and incorporated the influence of time-spatial distribution.

An important aspect in the effective use of a laser for tissue welding is the tissue radiation absorption index for a given wavelength. Typically, the radiation absorption index in tissue is described by the law of Bouguer, and absorption index values for above mentioned wavelengths have been published (12). Since the primary component of most tissues is water, the radiation absorption index for water is sometimes used to approximate spectral efficiency.

In medical applications the average tissue thickness is approximately 1.5 mm (tissue of small intestine). Therefore transmitting factors for a one-layer T1 and double-layer T2 tissue are rather useful for further evaluations. Their values show the

part of laser beam energy (power) being delivered to the interface of welded tissue pieces. It is necessary to note that the value of T2 factor can tend to be overestimated, as determined by the Bouguer's law, because laser beam dispersion at the interface is typically not taken into account.

In Fig. 3 spectral dependencies of these factors are shown. It can be seen that the maximum value for a double-layer transmitting factor T2 is reached at wavelength 1.06 μm and does not exceed 0.25 μm .

Laser tissue welding studies to date have typically used wavelengths in the range 0.63μm to 1.μm, presumably because 1) this range is highly supported with many types of medical lasers being produced commercially, including semiconductor, helium-neon and neodim (with the various additives) lasers, and 2) because tissue absorption tends to be smaller within this wavelength range, and wavelengths with this range tend to penetrate into the tissue more deeply.

Tissue portions to be welded typically provide a variety of different structural and morphological components. Inside the tissue layers discreet structures exist, including sensitive nerve endings, capillary blood vessels and a net of thin nerves, connecting these structures with each other and transmitting signals to and from the central nerve system. Changes within or in the relationship(s) between these various components can affect spectral characteristics, and in turn, tissue absorption characteristics, just as these components and characteristics can differ as between *in vitro* and *in vivo* applications.

Preferably a tissue welding laser of this invention is selected and used in a manner that maintains a desired laser radiation energy (power) at the welding zone. A preferred average tissue welding power density is between about 10 W/cm^2 and about 50 W/cm^2.

Specified power density can be achieved in any suitable fashion, and preferably in a manner that provides an optimal combination of laser radiation power and beam cross-section area at the welding zone. Laser beam power at levels higher than optimal can lead to technical and economical problems. For example, if the laser radiation power exceeds several watts it may be necessary to use a cooled fiber optical cable to deliver the radiation to the welding zone, thus increasing the complexity and

cost of the apparatus, as well as requiring that the user meet whatever relevant safety precautions may exist.

It is typically preferred, therefore, for reasons of efficacy, cost, and ease of use, to use a laser beam with minimal allowable cross section area. Thus the optimal power densities at the welding zone are reached without increasing the total power level, that results in significant reduction of safety requirements and the cost of the equipment. Usually the laser beam in a welding zone is formed by focusing optics. The transverse dimensions of the beam are provided in the focal cross-over zone and depend on laser beam divergence at the entrance of the focusing optics, it's focal distance and aberrations. Beam divergence for commercially produced gas and semi-conductor lasers, for instance, are typically in the range of about 3 mrad to about 4 mrad. If the focusing optics is aberrationless and it's focal distance, for example, is 5 cm, the transverse size of the laser waist should be about 0.015 cm to about 0.02 cm. If aberrations take place the size of laser waste may be much larger.

The use of short-focused aberration-free lenses, together with laser radiation having small divergence can reduce laser waste by up to about 0.0075cm to about 0.01 cm. It is thus possible to use lasers with lower power capacity while also expanding the range of variance by duration of exposure. Those skilled in the art, given the present description, will appreciate the manner in which the formation of an optimal laser channel, as well as the choice of spectral range, can be key features in the development of laser tissue suturing equipment.

EXAMPLE 2

Multispectral laser welding

Experimental equipment included laser radiation sources, focusing lenses, tissue fastening units as well as diagnostic devices, according to the functional schematic shown in Fig. 4. Laser sources identified as L1 -L3 were a conventional He-Ne gas laser, a semi-conductor laser, and a Nd laser, respectively. The He-Ne laser (Ll) with wavelength 0.63 µm was operated in a continuous mode. The average radiation power was 25 mW. Divergence of laser beam was 3 mrad. An electromechanical modulator (EMM) was used to control the laser beam exposure time. A variable duration pulse generator (PG) and a supplementary control unit (CU)

were used to control the EMM. The time of exposure could be varied in the range from 0.5 s up to several minutes.

The semi-conductor laser (L2, wavelength 0.68 μm) also worked in a continuous mode. Thus the average radiation power was 30 mW. Collimating optics provided semiconductor laser beam divergence on the order of that found with the He-Ne laser. An external pulse generator was used to modulate the laser beam pulse rate from units of Hz up to several tenfold of kHz and the duration of pulses - from a hundred nanoseconds (ns) up to hundred milliseconds (ms).

The Nd laser radiated a pulse mode at wavelengths of 0.53 μm and 1.06 μm. The pulse rate was controlled by an external pulse generator which could generate pulses in a unitary mode, and in a periodic mode with frequencies from 1 up to 5 Hz. The pulse duration was 20 ns. The pulse radiation energy was equal to 8 mJ. The beam divergence was 10 mrad. The power and timing parameters of laser radiation were supervised by diagnostic devices. The laser radiation was directed to diagnostic equipment by means of first and second beam splinters BS1 and BS2.

The average power capacity and energy of radiation were measured by means of a conventional device (HMO-2) . Measuring the pulse duration of a semi-conductor laser was achieved by means of a photo-electronic amplifier PR1 (on the basis of a silicon photo diode (ϕΠa-28) and oscilloscope OS1 of a type C1-94. Measuring of the Nd laser pulse duration was achieved by means of a photocoaxial amplifier PR2 of the type FEK-31 KP. It was connected to the oscilloscope (OS2) of the type C1-11 through a wave resistance matching unit. The laser beam focusing unit and tissue fastening unit were developed so that they could be used in the subsequent design of an equipment of laser tissue welding.

Traditionally the formation of a beam in a welding zone is accomplished by means of a short focal distance (several centimeters) lenses. Therefore a lens with small aberrations was used in focusing unit. The light aperture diameter was made 4 cm and the focal length 3.5 cm. The focusing unit was furnished with special technological rigging, enabling to supervise the location of the laser waist central part and to measure distribution of laser radiation in cross section area.

The fastening of tissue was accomplished by means of a specially developed technological unit, the simplified schematics of which is shown in figures 5a (top

view), 5b and 5c. This unit permits to influence tissue with a laser beam that has specified levels of the power density on a specified plane (point) of tissue. The unit includes two optical tables (1, 2) and a mandrel (3). Optical tables could be moved linearly at two orthogonal directions. Each table was supported with a scale (4, 5), enabling to determine linear displacement with step-type behavior 0.0025 cm. The mandrel (3) (Fig. 5b, 5c) has three windows (6), which are used for fastening the tissue, the fine-tuning element and an optical slit to measure the cross-sectional energy distribution of the laser beam. The specified elements were fixed in the mandrel by means of clamping springs (7). The cell for tissue disposition consisted of two flat-parallel quartz plates with thickness 0.1 cm and 0.5 cm. The spectral characteristics of the plates are shown in Fig. 6. The tissue under research was placed between these plates, the distance between the plates being fixed by means of precious gaskets. The quartz plates were chosen so that to ensure identical transmission factors (the constancy of the contribution of optical elements) in a wide spectral range.

Cross-sectional laser beam energy distribution at the laser beam waist has been obtained by means of the optical table (1) (Fig. 5a) together with an optical slit. The lightning size of the optical slit was equal 0.001 cm. A fine tuning element (mirror) was used to accomplish accurate placing of a certain zone of the laser waist on a specified tissue site. Fine-tuning was achieved by means of the optical table (2). In order to achieve supervision of the dynamics of tissue morphological changes during laser irradiation a site visualization system was developed. This system consisted of a CCD TV camera (type SK 1004) with a frame-grabber and a PC.

At an initial stage, the effect on the tissue surface by means of laser irradiation was investigated. In experiments the pieces of natural tissue were used. The tissue surface was placed within the laser beam laser waist. The cross section area size of the laser beam on the tissue surface constituted 0.015 cm. Thus at the laser influence zone the following power flow densities were achieved: He-Ne laser - 110 W/cm^2 , semi-conductor laser - 130 W/cm^2, Nd laser - 3 J/cm^2.

The received power characteristics appreciably exceeded allowable values of power densities for laser tissue welding indicated in (4). The duration of laser irradiation of the tissue surface has been varied in the range from several seconds up

to two minute. The radiation of He-Ne and semi-conductor lasers with above mentioned parameters did not cause any appreciable morphological changes on the tissue surface. Only the drainage of the tissue was observed. Radiation of He-Ne laser on a glass with neodim caused an electrical spark-over on the tissue surface, accompanied with a characteristic sound effect of the click type. The pulse frequency rate of laser radiation was changed from 1 Hz up to 5 Hz. Electrical spark-over arose with each pulse. However the laser effect has not resulted in any appreciable morphological changes of the tissue surface. Studies using a CO_2-laser have been also performed. Because of strong tissue surface absorption of radiation at the wavelength 10.6 microns only surface coagulation occurred followed by subsequent carbonization.

Though not optimal, the present findings demonstrate the potential utility of this approach, though clearly the laser power densities and/or wavelengths need to be opimized.

EXAMPLE 3

Experimental research of the tissue spectral characteristics.

A study of the spectral characteristics of tissue samples was performed in a wavelengths range from 0.1 microns up to 10.6 microns. Two spectrophotometers (MPS-2000 from Shimadzu, 0.19-0.9 microns, IR-435 from Shimadzu, 2.5-10.6 microns) were used to measure reflection and transmission indexes of researched materials. All listed devices were developed on the two-beam basis the tuning and measurements being accomplished with microprocessors.

In Figs. 7 and 8 the optical circuits of MPS-2000 and U-3400 are shown. In model MPS-2000 a Cerny-Turner monochromator is used. In Model U-3400 a double monochromator is used as well as a photomultiplier (spectral range 0.19-0.9 microns) and a PbS photoconductor (spectral range 0.9-2.5 microns). To conduct measurements of specular and diffuse reflection indices both monochromators were equipped with special supplementary units which schematics are shown in Figs. 9 and 10. The multitarget unit RTA-2000 (Fig. 9) was used to proceed measurements of tissue diffuse reflection index in the wavelength range 0.19-0.9 microns the comparison method on an integrating sphere being applied. The latter was coated

with $BaSO_4$. A piece of fresh-pressed $BaSO_4$ powder was used as a reference sample. The integrating sphere and the mirror optics system of the supplementary unit are installed in the measuring channel of the microphotometer. The latter is by means of electronics compared with a reference channel.

Fig. 10 shows the optical circuit of spectral photometer IR-435 to be used in medium IR radiation range. The spectral measurements were based on a method called the optical zero, which is established by an optical wedge, entered in the reference channel of the spectral photometer. Such a circuit is more preferable for the medium IR range since the linearity and dynamic range of the photometry measurements are higher.

A distinctive feature of applied absorption index measuring technique is that in all measurements the same cell for tissue disposition was used. The spectral characteristics of source and target windows of a cell are shown in Fig. 6. The thickness of the cell was chosen to ensure identity for the tissue samples being used in experiments on laser welding. The double thickness of a tissue sample is 0.3 cm. In the case when the influence of tissue thickness on its spectral characteristics was investigated the sample thickness was changed from 0.13 cm up to 0.15 cm.

On external view investigated samples were characterized as follows. The surface tissue layer is transparent with distinctive whiteness. No greasy stains are present. For spectral studies, double layer tissue composition was used, i.e., two pieces of tissue with thickness 0.15 cm folded together side by side. The results of reflection, transmission and absorption indices spectral measurements for double layer tissue samples are presented in Fig. 11.

The graph of the reflection index has distinctive oscillations in the short-wave spectral range 0.2-0.4 microns. This phenomenon appears to be due to some features of excitation in organic compositions. The values of indices in this range do not exceed 0.2. In the wavelength range 0.5 - 0.6 microns the fluctuations of the reflection index are essentially less than in the shortwavelength range. The average value for the reflection index is 0.14. In the near IR range (0.6-0.9 microns) the reflection index does appear to depend on wavelength and its value is 0.2.

A distinctive feature in behavior of a transmission index is its extremely low values for wavelengths less than 0.4 microns and appreciable increase in the range

0.4-0.9 microns. Maximum value of transmission index is achieved at wavelength 0.9 microns and is 0.38. It could be seen from Fig. 11, that the transmission index for investigated tissue samples strongly enough (~5 times) differs from the same index considered in (12).

The absorption indices were calculated being based on the results of reflection and transmission indices measurements. The results are shown in Fig. 11. The analysis of the indicated graph shows, that the tissue has reasonably large absorption index (0.85) in the wavelength range 0.2-0.4 microns. On wavelengths from 0.4 microns up to 0.82 microns the value of absorption index decreases down to 0.38. Between 0.82 and 0.9 microns its value is almost constant.

Also the influence of tissue density on the absorption index was investigated. Samples compressed to the half of their original thickness were investigated. The results of these experiments are shown in Fig. 12. From this figure it could be seen, that the spectral characteristics of compressed tissue in the investigated wavelength range do not practically differ from those for the samples with original thickness.

The results of the tissue spectral characteristics research in the IR-range (2-25 microns) are shown in Fig. 13. The transmission index was equal to 0 practically in the whole wavelength range and the reflection index was of an order of a few percents. In a region besides wavelength 3.3 microns an oscillatory spectrum of a water was found. The seemed increase of the reflection index at wavelengths above 4 microns is stipulated by sample heating with IR irradiation and the beginning of it's own radiation.

EXAMPLE 4

Experimental research on laser tissue welding

The results of spectral research demonstrated that tissue is relatively transparent and consequently visible and near-IR laser radiation penetrates into the tissue deep enough. Since laser radiation passes through tissue with close-to-light speed optical power enters the tissue almost instantly. Therefore the heating of tissue begins simultaneously on the whole volume. In a central zone of the beam with the high power density tissue evaporation occurs. On the periphery of the beam fusion of tissue takes place. In our researches the ratio between thickness of the welded tissue and the size of cross section of the beam was approximately 6/1. Therefore

apparently the uniformity of energy contribution into the welding zone is determined mostly by the laser beam power density distribution along the laser beam axis. If energy contribution along the beam is uniform the differences of mechanical tension in welded tissue should be minimum. Thus apparently the conditions for sound tissue welding should be best provided. Obviously, this condition inside the tissue would be fulfilled if the changes of the power density along the beam axis are small. If this assumption is valid the choosing of preferable laser radiation wavelength must take into account the shape of the laser beam entering the tissue.

One can assume that the scattering of laser radiation in tissue is insignificant in relation to absorption. Besides we shall consider that the change of laser radiation power along the tissue depth is subject to the law of Bouguer. Considering the power density distribution in tissue at different laser radiation wavelengths in the cases of focused and unfocused beam. The experimental data indicated in section 4 is being used. Considering the focused beam we shall assume, that the diameter of the beam at the entrance of focusing optics is 2 cm, focusing distance is equal 5 cm, and the cross section of laser waist is 0.03 cm.

The power flow density was evaluated in an arbitrary tissue cross-section *P(x)*, referred to power density on the tissue surface P_o, for wavelengths 0.5 microns, 0.6 microns, 0.7 microns and 0.9 microns. The results of calculations for an unfocused and focused laser beams are shown accordingly in Fig. 14 and Fig. 15.

As it could be seen from Fig. 14 for an unfocused beam the more preferable radiation wavelength is 0.9 microns. With reduction of radiation wavelength the gradient of the power density along the laser beam grows. The largest gradient is observed at wavelength 0.5 microns. The apparent advantage of near-IR radiation is connected with one rather essential problem. Appointed spatial distribution could be formed in the long-focus mode. In this mode the size of a beam in the focal zone is essentially larger, than in the short-focus mode. Therefore for optimum maintenance of energy contribution it is necessary to increase the exposure duration or the laser power. The former causes a decrease in welding speed and the latter increases the complexity of equipment maintenance. The increase of exposure reduces speed of laser welding while an increase in laser radiation power complicates devices for laser tissue welding.

In the short-focus mode (Fig. 15) the more uniform power density distribution is provided on a wavelength equal to 0.5 microns. With wavelength increase the gradient of power density along the laser beam grows. It is obvious, that this case of radiation in visible range 0.5-0.6 microns is more preferably, than near-IR. It should be noted, that in the short-focus mode it is possible to ensure high power densities with a rather less powerful laser. Therefore this range is more preferable for laser tissue welding.

Among commercially produced lasers ensuring reasonably enough power in the wavelength range 0.5-0.6 microns, argon, xenon, krypton lasers and lasers on copper vapor should be mentioned. The former type radiates in the wavelength range 0.49-0.51 microns and delivers a few watts of power. The latter delivers several dozens watts of power in the range 0.51 up to 0.578 microns.

Further researches were performed with a copper vapor laser delivering maximum mean power 20 W in a periodic pulse mode of operation. The pulse rate frequency is up to 10 kHz, pulse half-width duration was 20 ns, beam diameter at the focusing optics entrance was 2 cm, beam divergence - 2 mrad. Exposure time is provided by means of a mechanical diaphragm.

A single channel functional scheme of experimental equipment shown in Fig. 4 was applied. The beam focusing unit and the tissue fastening were the same, as in researches on multispectral experimental equipment. Since the laser operated at a two wavelength pulse-periodic mode the equipment for diagnostics differed from the equipment, applied in multispectral research.

Experiments were performed with two focusing modes: long focusing distance and a short one. In the long focusing mode the focusing distance of a lens through which the tissue was irradiated, was chosen equal to 50 cm. The diameter of the laser waist was 0.08 cm. In the short focusing the focal distance was equal to 5 cm, and the diameter of a focused spot was 0.03 cm. The characteristic laser beam power distribution curve at the laser waist for this mode is shown in Fig. 16. It was obtained by scanning the waist with an optical slit. The asymmetry of the radiation intensity distribution is caused by significant aberrations being the consequence of poor quality of the focusing optics.

In the long focusing mode experiments were performed with laser radiation power equal to 4 W. The exposure time was varied from 20 s up to 130 s. The power density on the tissue surface was equal to 625 W/cm^2. In all cases tissue burn-through-has been registered. No tissue welding was observed. The image of a tissue sample being influenced with laser irradiation during 20 s is shown in Fig. 17. The area where the -laser beam has been interacting with the tissue is brightly characterized by an expressed hole through the tissue and a peripheral zone around it. The inner walls of the hole are carbonized.

With the short focusing mode experiments were carried with the radiation power 10.8 W. The exposure time has been varied from 1.5 with up to 30 s. The power density on the tissue surface was equal to 3.0 kW/cm^2 . Tissue samples were investigated at following exposure duration: 2 samples - at 1.5 s, 7 samples - at 5 s, 1 sample - 10s, 5 samples - 20 s, 1 sample - 30 s.

The tissue burn-through and welding were registered in all cases. In Fig. 18 - 20 sample tissue images are shown being influenced by a laser beam at the exposure time intervals 1.5, 5 and 20 s. It could be seen that with an exposure duration increase the burn-through hole diameter is increased. At the exposure duration's 1.5 and 5 s on the contrary of the case of 20 s exposure no carbonization has been registered.

The tissue area in a vicinity of the burn-through hole had three characteristic zones: a purely burn-through zone and two ring zones. The burn-through zone is represented by a circular open-through aperture, which size depends on the exposure time. For exposure times 1.5, 5 and 20 s the aperture diameter measured accordingly 1, 1.5 and 2.5 mm. The periphery of the burn-through hole (internal wall) at exposure times 1.5 and 5 s had characteristic hardening caused apparently by tissue coagulation. At the exposure time 20 s carbonization was observed on the periphery of the burn-through zone.

The first and the second ring zone in all cases looked like a kind of concentric rings. The sizes of these rings for all investigated exposure times were roughly identical. The outer diameter of the first ring measured 3.0-3.5 mm, and outside - 4.3-4.8 mm. On appearance the tissue morphology within the second ring did not differ from the tissue, not subjected to the effect of laser radiation. The first ring was characterized by a prominence and it's surface looked like being coated with a glass-

like film. The thickness of the glass-like film was by the order of 0.1 - 0.2 mm. The prominence amplitude did not exceed 0.2 - 0.3 mm for the tissue sample being exposed at 5 s. The amplitude of the first ring for a tissue sample being exposed at 20 s was 1.5 - 2 times larger. The second ring was characterized by a weak cavity the amplitude of which at exposure time 5 s did not exceed 0.2 mm.

The firmness of the welding area has been checked by tearing the welded tissue pieces the force equal to 15 g being applied. Fig. 21 shows a tissue sample being under the test of welded suture firmness. The suture exposed at 1.5 s has appeared to be weak, sutures exposed at 5 and 20 s were had sustained forces applied to them.

Comparing experimental results, received in long and short focus modes, it is possible to note the following. Although energy contribution factors in long and short focus modes at 5-s exposure time are close in their values (12.5 and 15 kJ/cm^2) the tissue welding has been registered only in the short focus mode. Apparently, as well as it was assumed in part 5.1, an important item for tissue welding is the spatial power flow density distribution along the laser beam.

When tissue is being heated up to temperatures 58-65°C (13, 32) a process of protein denaturation begins. As far as it is marked in (32), the mathematical model of tissue with constant thermophysical properties satisfactorily describes the temperature field in it up to 75'C. Apparently, the denaturation process does not render essential influence on the tissue thermophysical properties. Thus, at the first approach (approximation) it is possible to assume, that the denaturation process does not render influence on a temperature field in tissue and from this point of view taking into account its influence is not necessary. On the other hand, referring to (12) exactly this process determines the firmness of a welded suture (in the welding zone a degree of denaturation should be as much as possible) and irreversible changes occurring in tissue being heated.

At further heating of tissue its temperature at some moment exceeds 100°C, therefore boiling of the in-tissue water begins. Strictly speaking, the drainage of tissue because of water evaporation also occurs at temperatures below 100°C (3, 9) and this process is to be taken into account from the very beginning of heating. However the account of a drainage process is rather complicated, because it is

necessary to calculate the transfer of moisture as well as the heat transfer. Besides the tissue parameters necessary for this calculation should be determined. On the other hand, as a rule, the power capacity of a laser used for tissue welding is rather large and the process of heating occurs very quickly. Therefore -at the first approximation the account of the in-tissue water evaporation is accomplished with a quasi-stationary adiabatic approach. It is assumed that if the temperature of any element, T_{ij}, has exceeded 100°C, boiling of the in-tissue water begins, continued up to it being completely evaporated from this element. The generated vapor goes outside the welding zone without interacting with other elements.

Applicants have demonstrated the ability to obtain a firm tissue weld using two fragments of a thin intestine tissue. Preliminary experimental results have shown that such a connection can be achieved using reasonable exposure energies and times. Visual inspection of the tissue surface at the welding zone did not reveal any undue structural changes outside a small zone of welding.

While the invention is susceptible to various modifications and alternative forms, specific embodiments thereof have been shown by way of example in the drawings and herein be described in detail. It should be understood, however, that it is not intended to limit the invention to the particular forms disclosed, but on the contrary, the intention is to cover all modifications, equivalents, and alternatives falling within the spirit and scope of the invention as defined by the appended claims.

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CLAIMS

What is claimed is:

1. A method for joining adjacent tissue portions using lasers, the method comprising the steps of forming a plurality of non-contiguous laser formed elements along a weld line, the elements being positioned in a predetermined pattern with respect to each other and each having a predetermined cross-sectional configuration.

2. A method according to claim 1 wherein the elements are independently created in order to achieve a desired absolute and relative extent of denaturation, coagulation, and/or carbonization within the tissue and particularly within the individual elements themselves.

3. A method according to claim 1 wherein the laser energy and/or exposure time are controlled in order control one or more properties selected from the extent of protein denaturation, dehydration, coagulation, thermolysis, and carbonization.

4. A method according to claim 3 wherein the net effect on tissue is assessed by determining the absolute and/or relative extent of denaturation, coagulation, and carbonization.

5. A method according to claim 1 wherein the method comprises the steps of

a) contacting two or more tissue portions, in a manner that provides respective surfaces of the tissues in direct or indirect contact with each other, such that the contacted tissue portions provide at least one surface accessible to a source of laser energy;

b) providing a source of laser energy; and

c) applying energy from the laser source to the accessible surface of the contacted tissues in manner that provides an optimal combination of;

i) the number and relative pattern of elements along a weld line;

ii) the cross-sectional structure of the individual elements along the weld line; and

iii) tissue impact within and surrounding each element.

6. A method according to claim 5 wherein the tissue impact is assessed in terms of the absolute and/or relative extent of denaturation, coagulation, and/or carbonization within each element and/or surrounding tissue.

7. A method according to claim 5 wherein the tissue portions are provided in a directly overlapping or abutting relationship with respect to each other.

8. A method according to claim 5 wherein the tissue portions are provided in an indirectly contacting relationship by the use of a secondary material.

9. A method according to claim 8 wherein the secondary material comprises an intermediate or surrounding layer of an exogenous treated natural tissue that is itself susceptible to laser radiation in order to form an integral bond with tissue portions to be welded.

10. A method according to claim 5 wherein the predetermined weld line is provided in a primary pattern selected from the group consisting of straight lines, zigzag, and wave forms.

11. A method according to claim 10 wherein the weld line further includes one or more secondary patterns formed in predetermined positions along a weld line.

12. A method according to claim 11 wherein the primary and secondary patterns are provided in a manner selected from: (a) the use of pattern-imposing masks, (b) the use of pattern positioned solder, and/or (c) in a controlled manner by controlling the location and other relevant parameters of the laser head itself.

13. A method according to claim 5 wherein the cross-sectional configuration of the elements is independently selected from the group consisting of elements of a generally cylindrical, multilateral, pyramidal, conical or egg shaped configuration.

14. A method according to claim 13 wherein the elements are solid through their entireties and are formed substantially at or near the interface between two tissue portions, so as to minimize the impact and possible trauma to surrounding tissue.

15. An apparatus for use in a method according to any previous claim, the apparatus comprising a hand-held or automated laser instrument having a laser delivery tip adapted to deliver laser energy in the form of impulses to the tissue, the

apparatus being adapted to create either a single point or patterns of such points in the sutured tissue.

16. An apparatus according to claim 15 wherein the tip is changeable by physically changing the tip itself or by altering computerized instructions thereto, in order to create different point patterns.

17. An apparatus according to claim 16 wherein the tip provides a pre-defined point pattern selected from the group consisting of arcs, triangles, a plurality of points in a row, or a single point.

18. An apparatus according to claim 17 wherein the tip is adapted to be used in either a variable and controllable mode and/or in a mode where the device is one or more fixed positions in order to be moved around the tissue.

19. An apparatus comprising a hand-held or automated laser instrument having a laser delivery tip adapted to deliver laser energy in the form of impulses to the tissue, and adapted to create either a single point or patterns of such points in the sutured tissue, wherein the apparatus is adapted to be used in a method comprising the steps of:

a) contacting two or more tissue portions, in a manner that provides respective surfaces of the tissues in direct or indirect contact with each other, such that the contacted tissue portions provide at least one surface accessible to a source of laser energy;

b) providing a source of laser energy comprising the apparatus; and

c) applying energy from the tip of the apparatus to the accessible surface of the contacted tissues in manner that provides an optimal combination of;

i) the number and relative pattern of elements along a weld line;

ii) the cross-sectional structure of the individual elements along the weld line; and

iii) tissue impact within and surrounding each element.

20. An apparatus according to claim 19 wherein the apparatus is adapted to assess tissue impact in terms of the absolute and/or relative extent of denaturation, coagulation, and/or carbonization within each element and/or surrounding tissue.

21. A system for joining adjacent tissue portions using lasers, the system comprising a laser radiation source and radiation transport component comprising an

apparatus according to claim 15 and one or more components selected from the group consisting of: one or more welding clamps; a cooling component with optics and sensor protection; a diagnostic component system; and an automatic welding control.

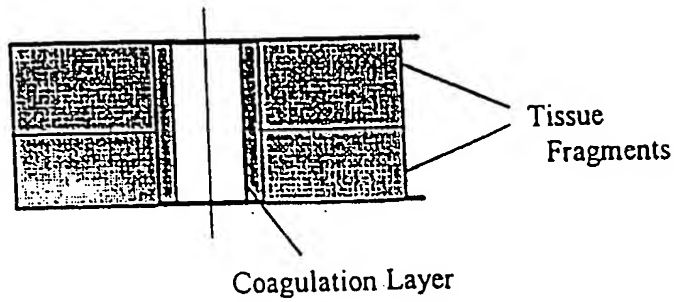


Figure 1a

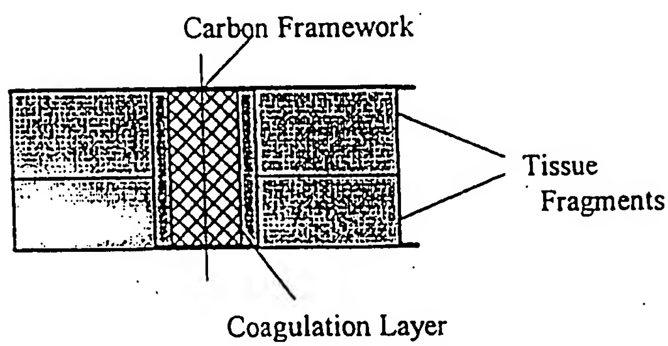
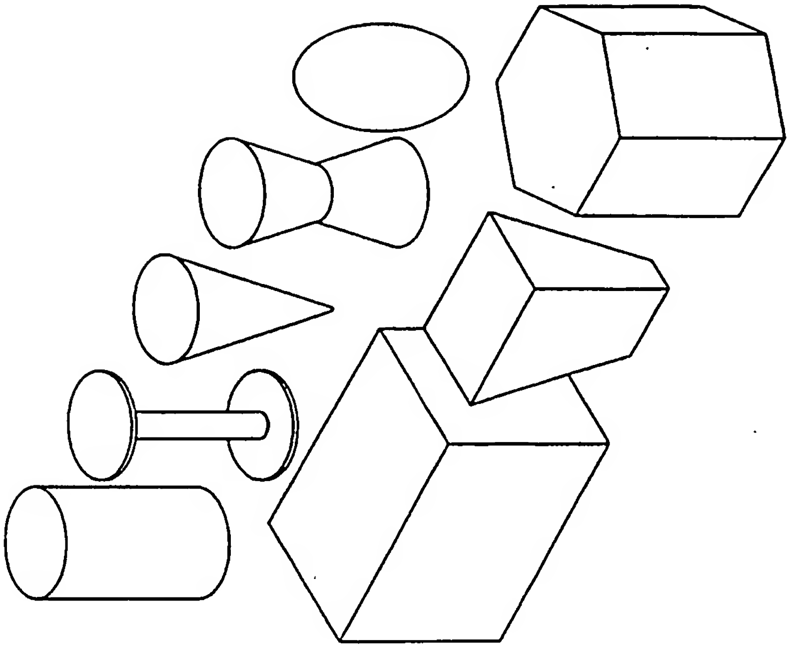
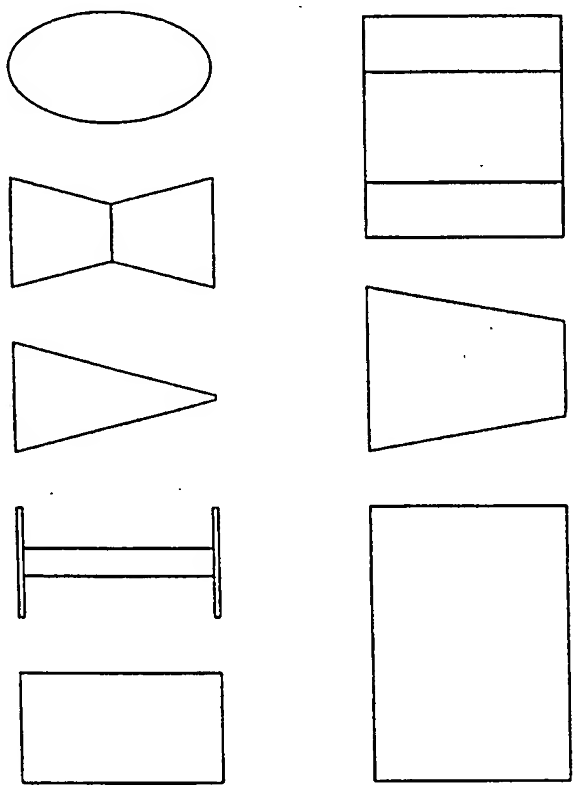
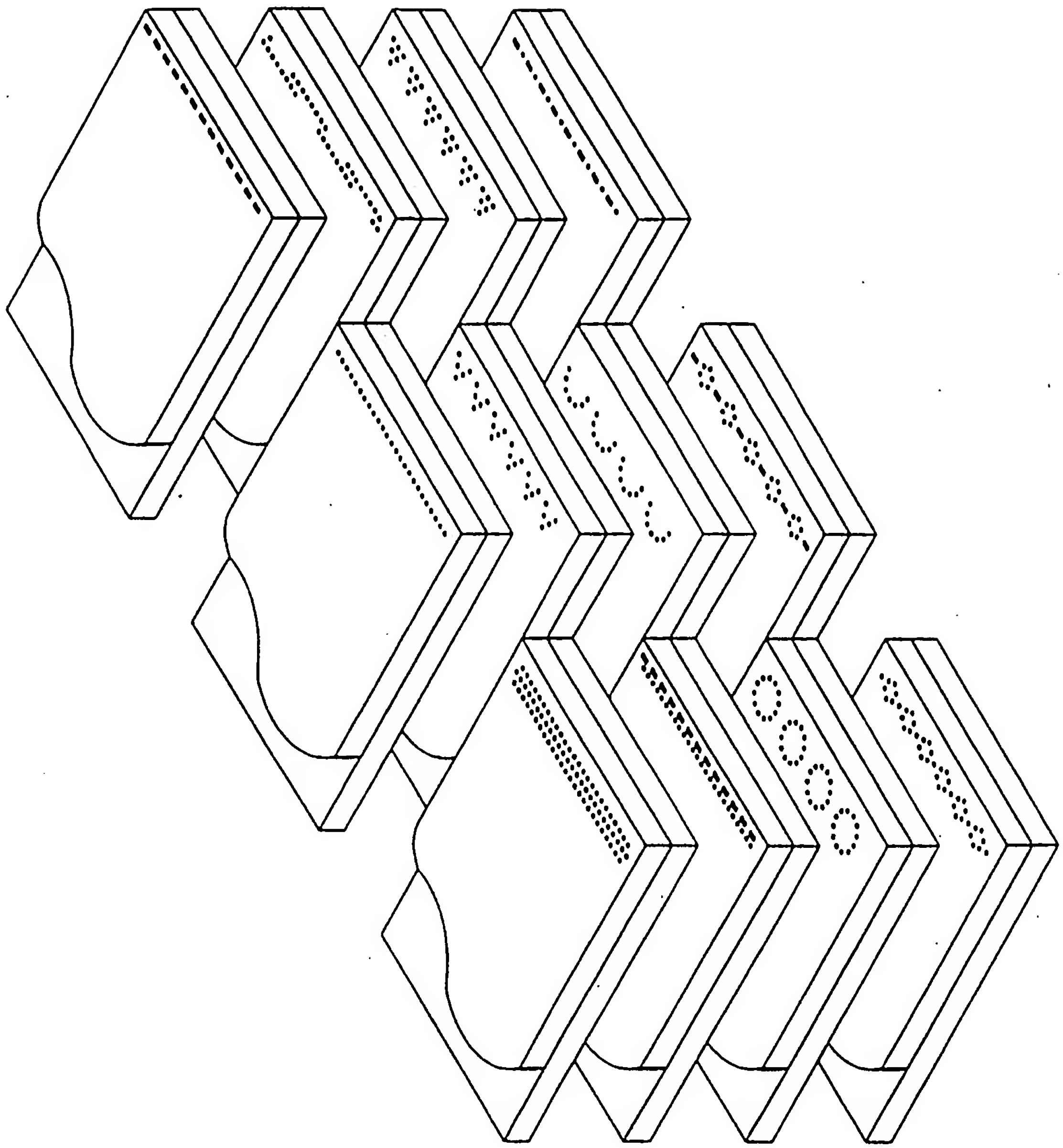


Figure 1b





2a



2b

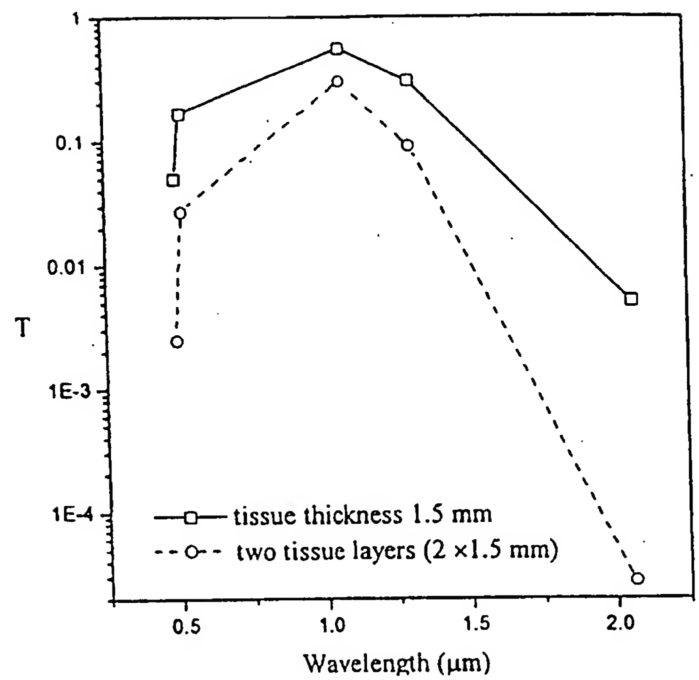

1
0.1
0.01
T
1E-3
1E-4
tissue thickness 1.5 mm
two tissue layers (2 ×1.5 mm)
0.5
1.0
1.5
2.0
Wavelength (μm)

Figure 3

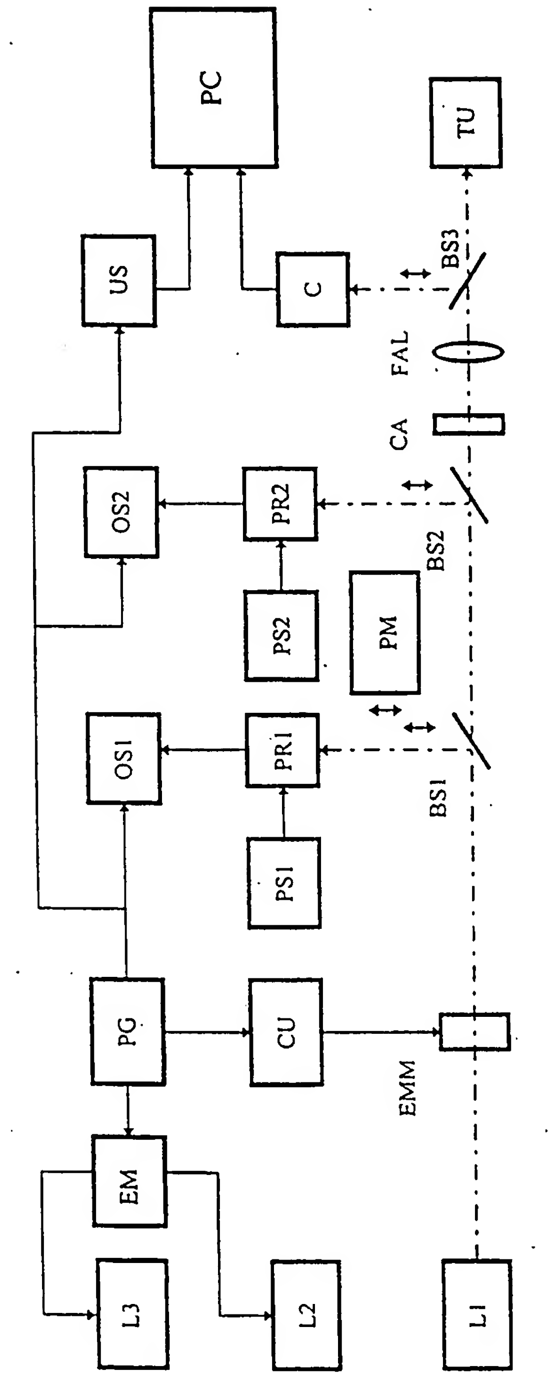


Fig. 4

L1 – laser (λ=0.63 μm); L2 – laser (λ=0.68 μm); L3 – laser (λ_1=0.53 μm, λ_2=1.06 μm); EMM – electro-mechanical modulator; CU – control unit; PG – pulse generator; EM – electronic modulator; BS1, BS2, BS3 – beam splitters; PR1, PR2 – photo-electronic amplifier; PS1, PS2 – power supply unit; OS1, OS2 – oscilloscope; CA – controlled aperture; FAL – free aberration lens; TU – technological unit; C – CCD camera; US – synchronization unit; PC – computer; PM – power measuring device.

Figure 4

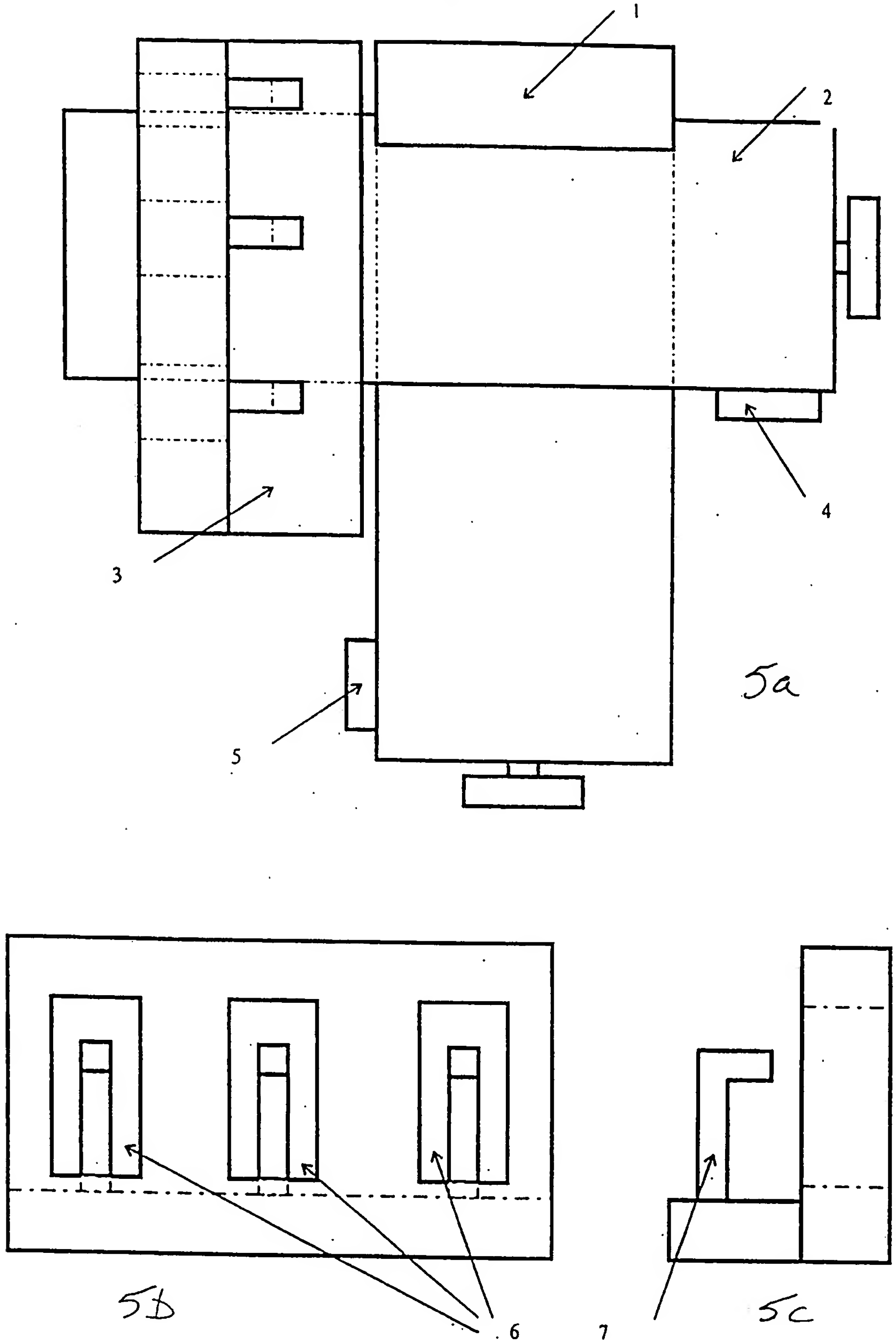


Figure 5

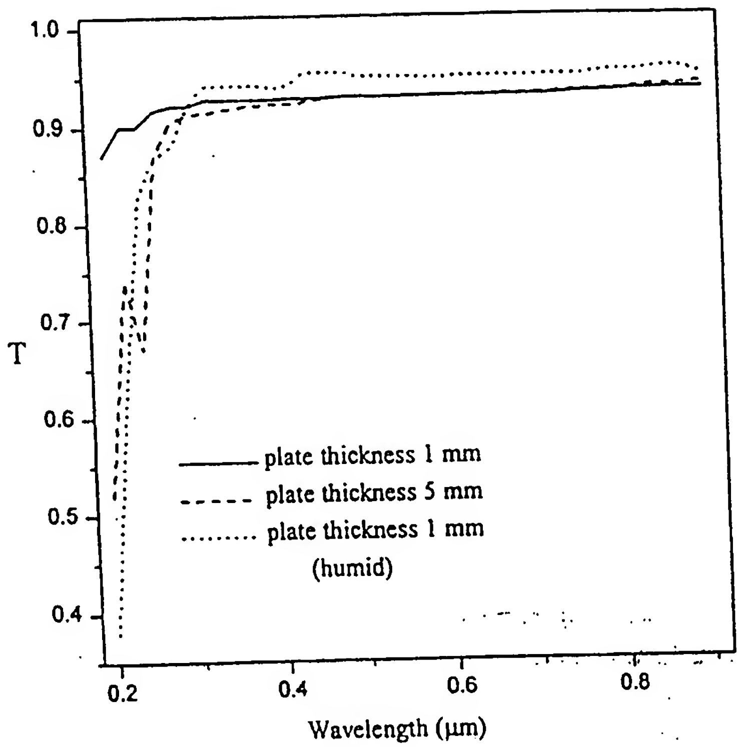

1.0
0.9
0.8
0.7
0.6
0.5
0.4
T
0.2
0.4
0.6
0.8
Wavelength (μm)
plate thickness 1 mm
plate thickness 5 mm
plate thickness 1 mm
(humid)

Figure 6

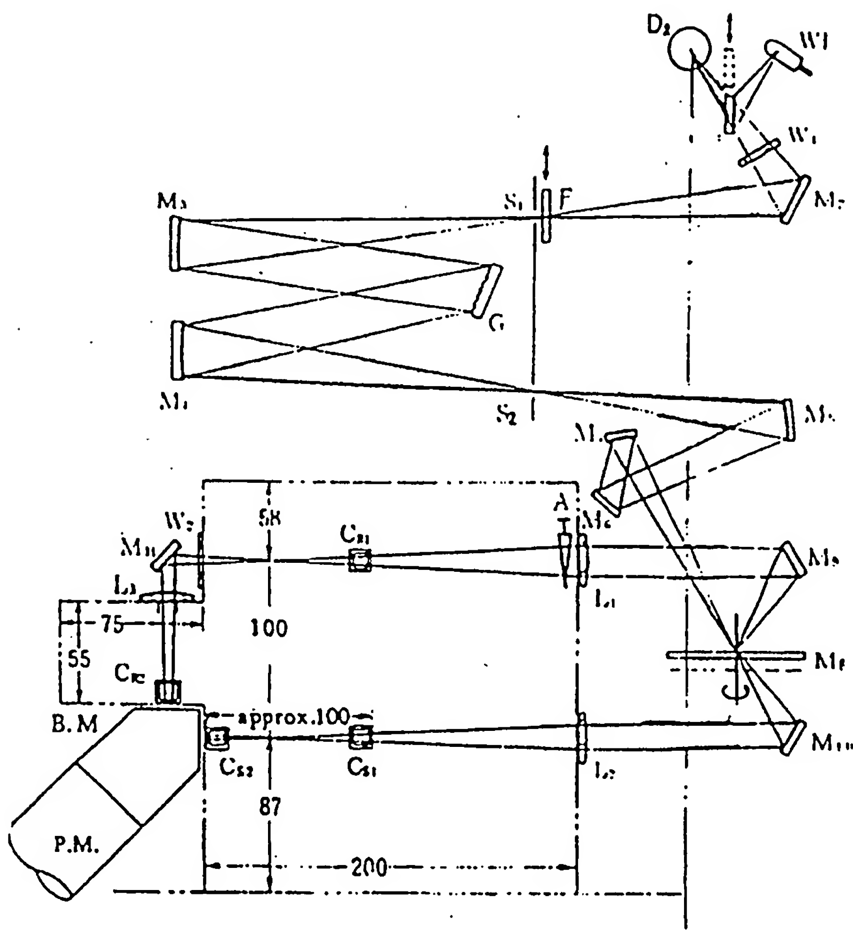

D2
W1
W1
M7
S1
F
M3
G
M1
S2
M5
M6
A
58
W2
M11
Cs1
L1
M8
L3
75
100
55
CR
MF
B.M
approx.100
M10
Cs2
Cs1
L2
87
P.M.
200

Figure 7

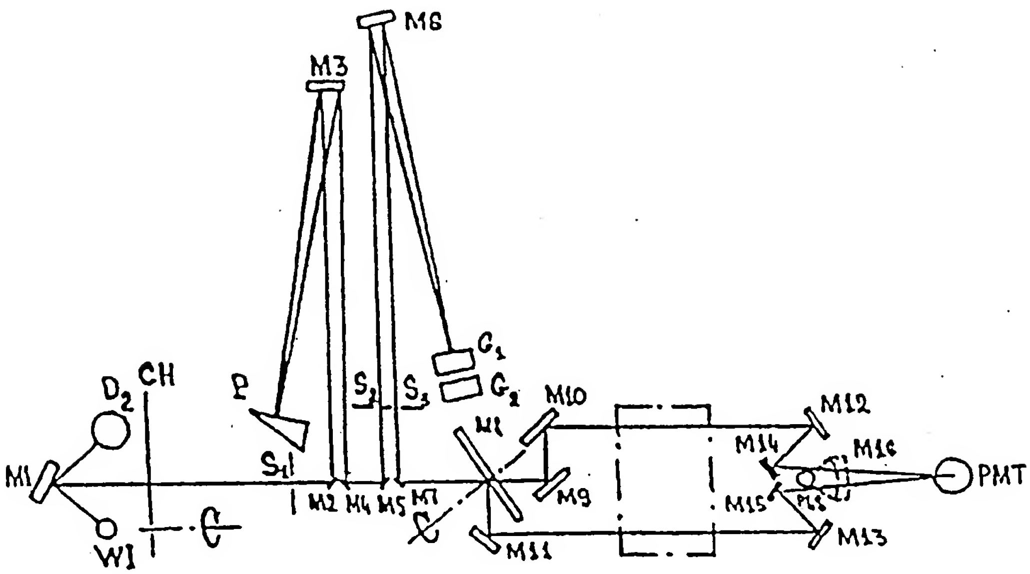

M8
M3
G1
G2
D2
CH
P
S2
S3
M10
M12
M1
M14
M16
S1
PMT
M2
M4
M5
M7
M9
M15
M13
M11
WI

Figure 8

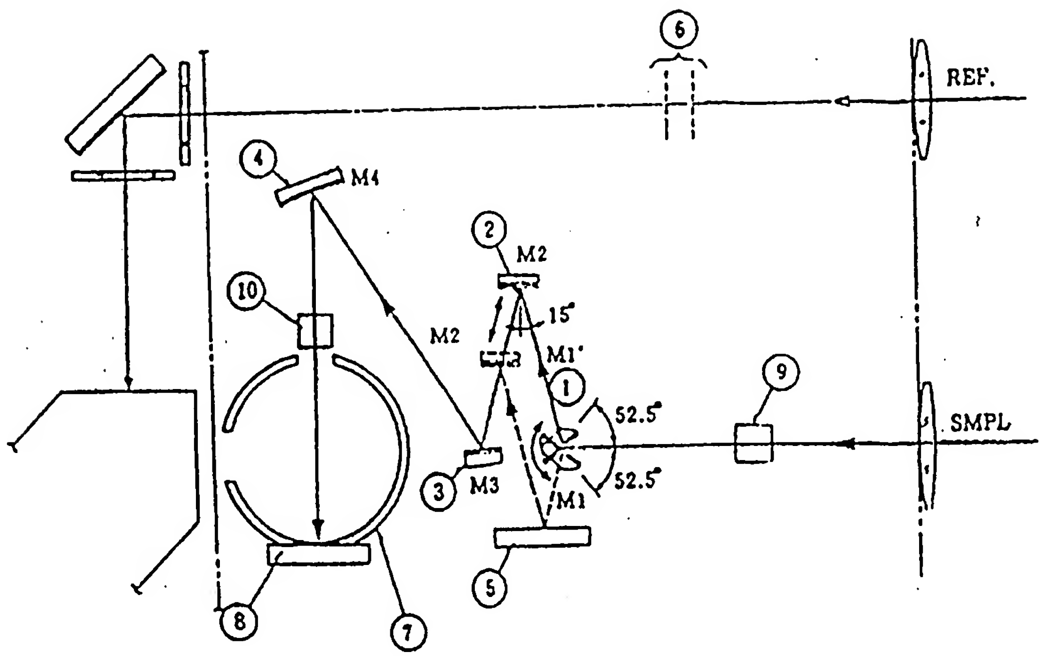


Figure 9

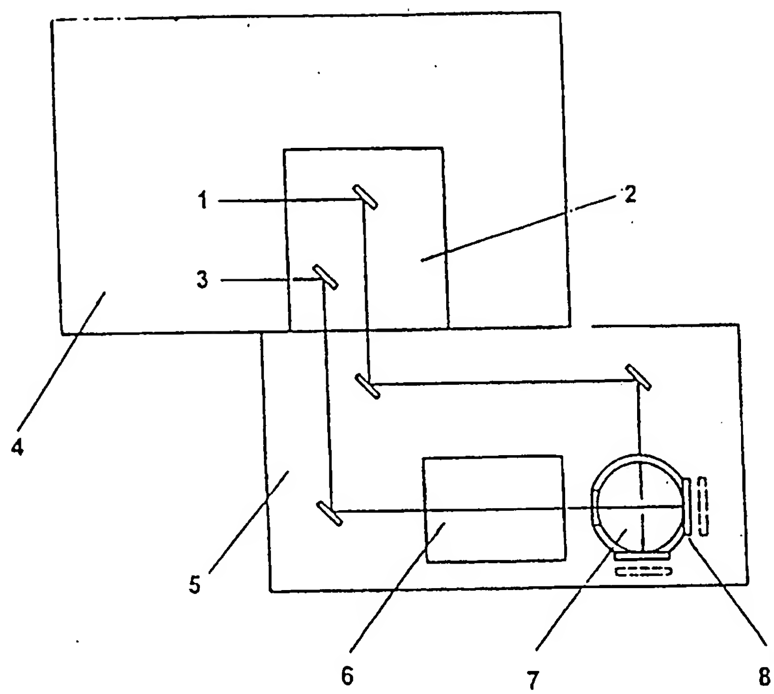


Figure 10

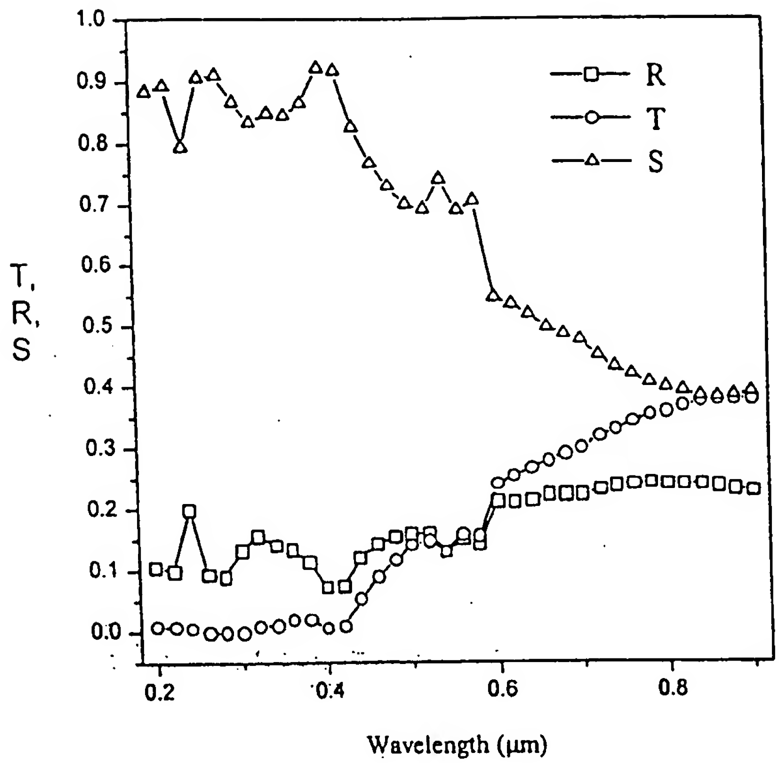


Figure 11

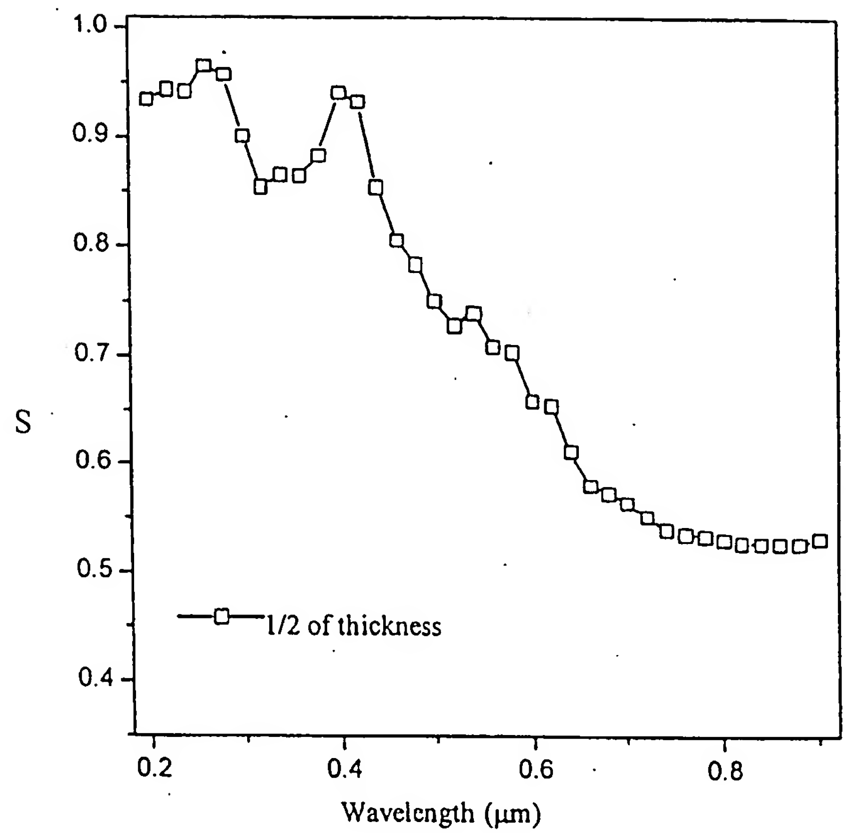


Figure 12

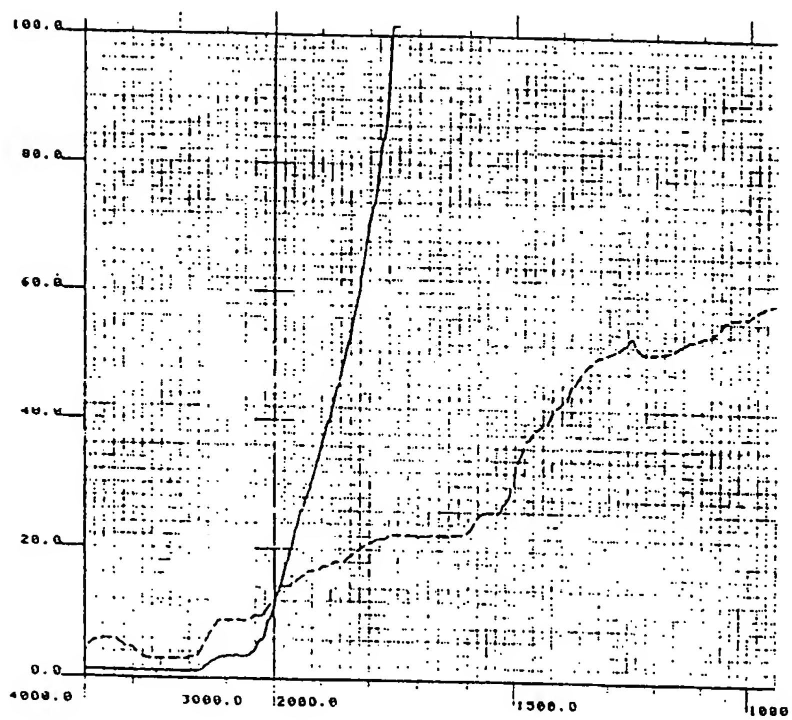


Figure 13

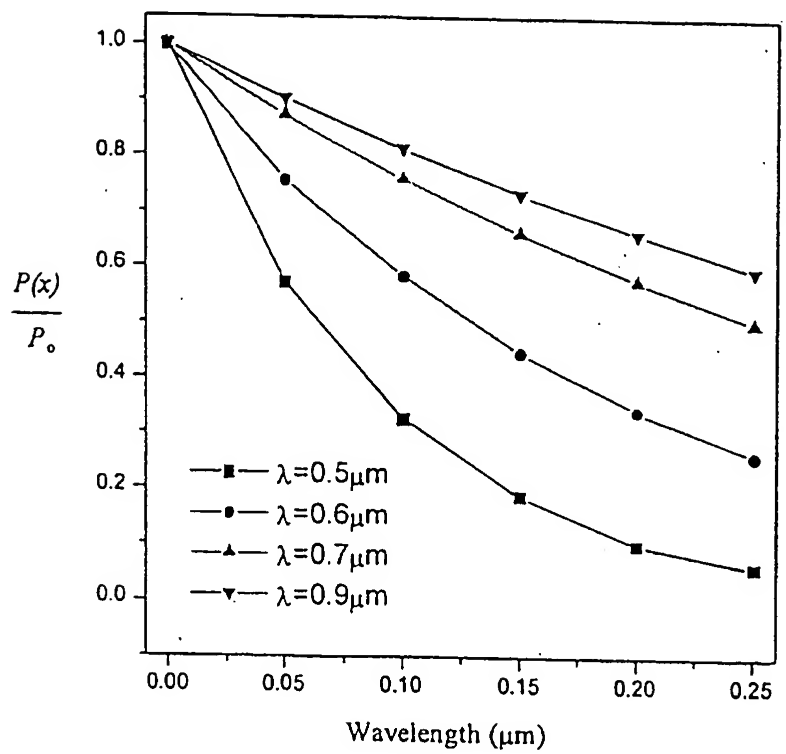

1.0
0.8
0.6
0.4
0.2
0.0
P(x)
P∘
λ=0.5μm
λ=0.6μm
λ=0.7μm
λ=0.9μm
0.00
0.05
0.10
0.15
0.20
0.25
Wavelength (μm)

Figure 14

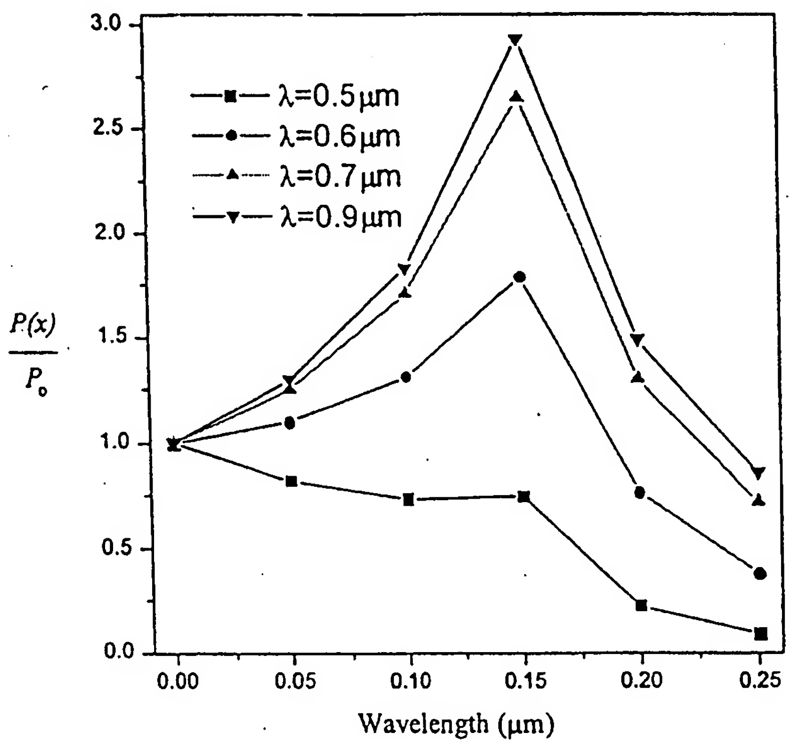

3.0
2.5
2.0
1.5
1.0
0.5
0.0
λ=0.5μm
λ=0.6μm
λ=0.7μm
λ=0.9μm
P(x) / Po
0.00
0.05
0.10
0.15
0.20
0.25
Wavelength (μm)

Figure 15

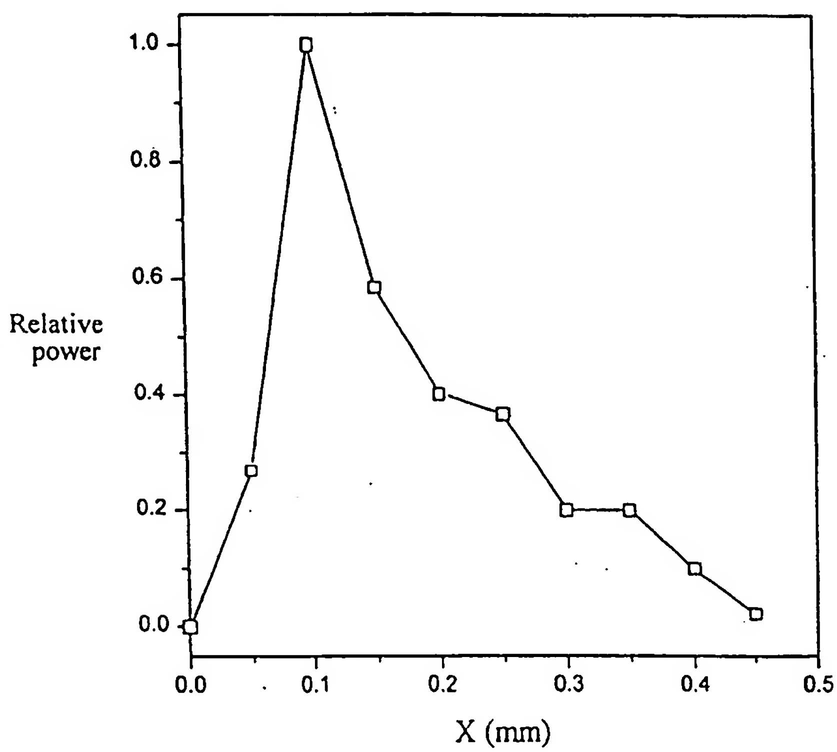


Figure 16

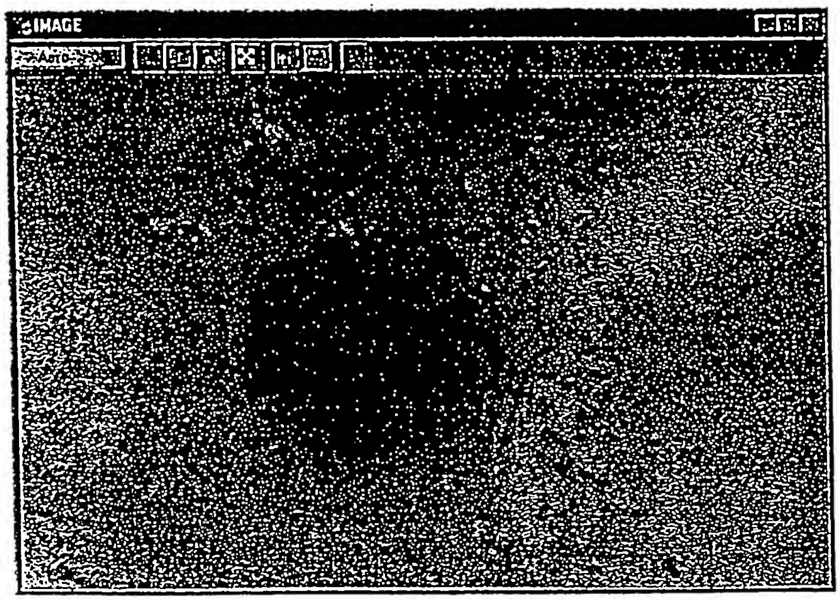


Figure 17

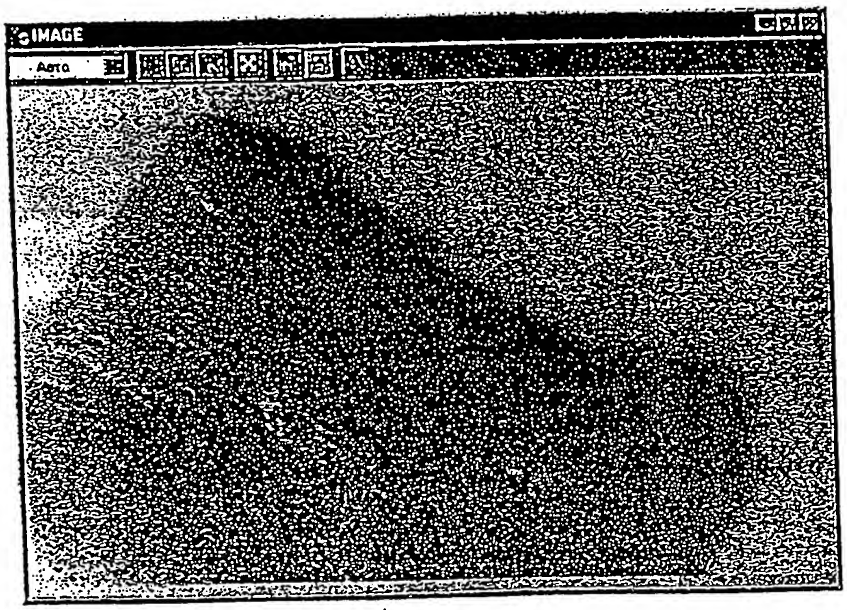


Figure 18

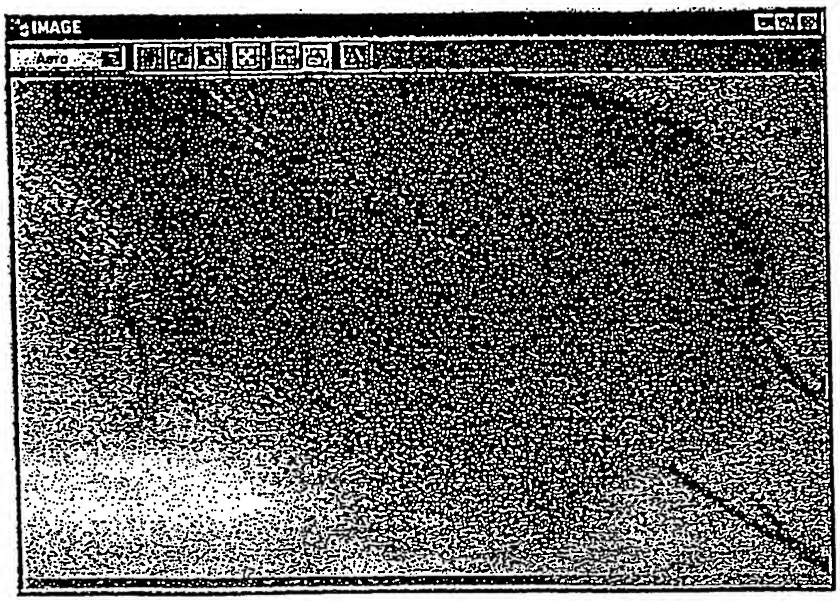


Figure 19

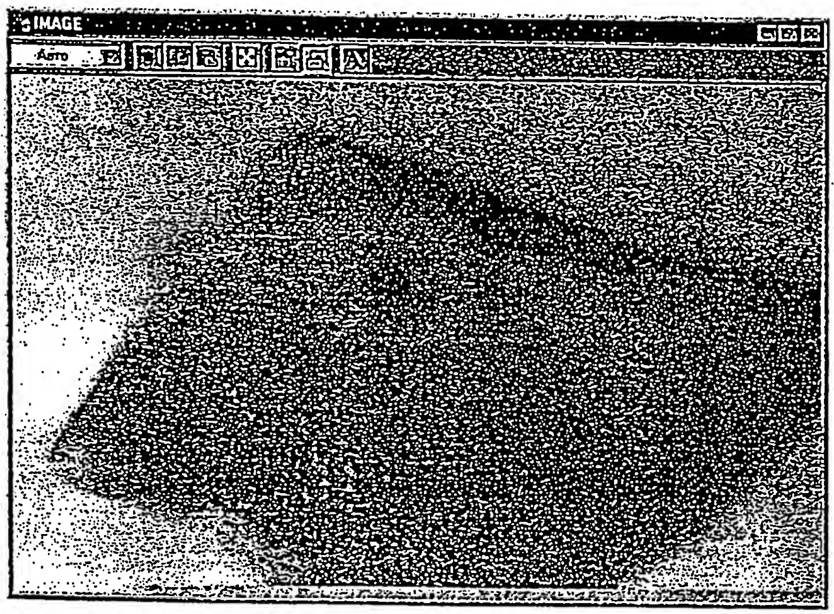


Figure 20

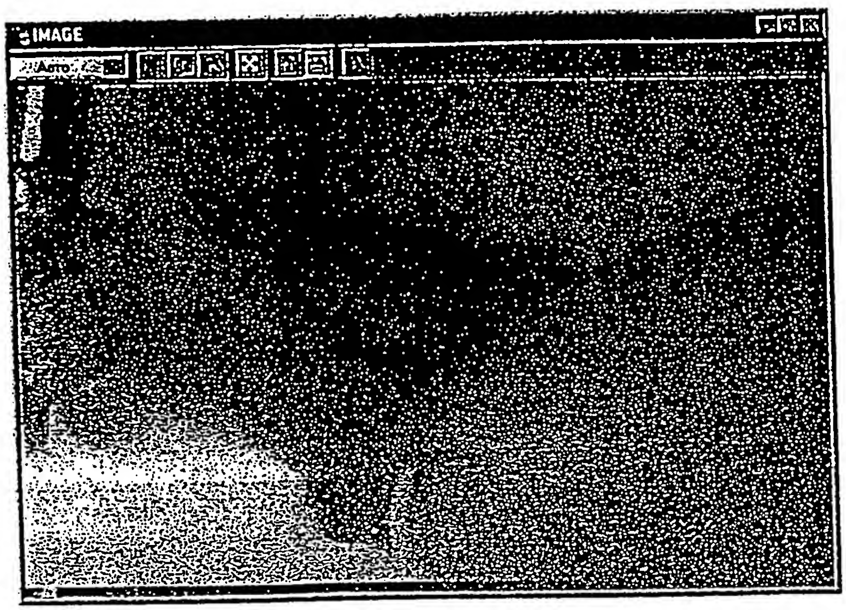


Figure 21

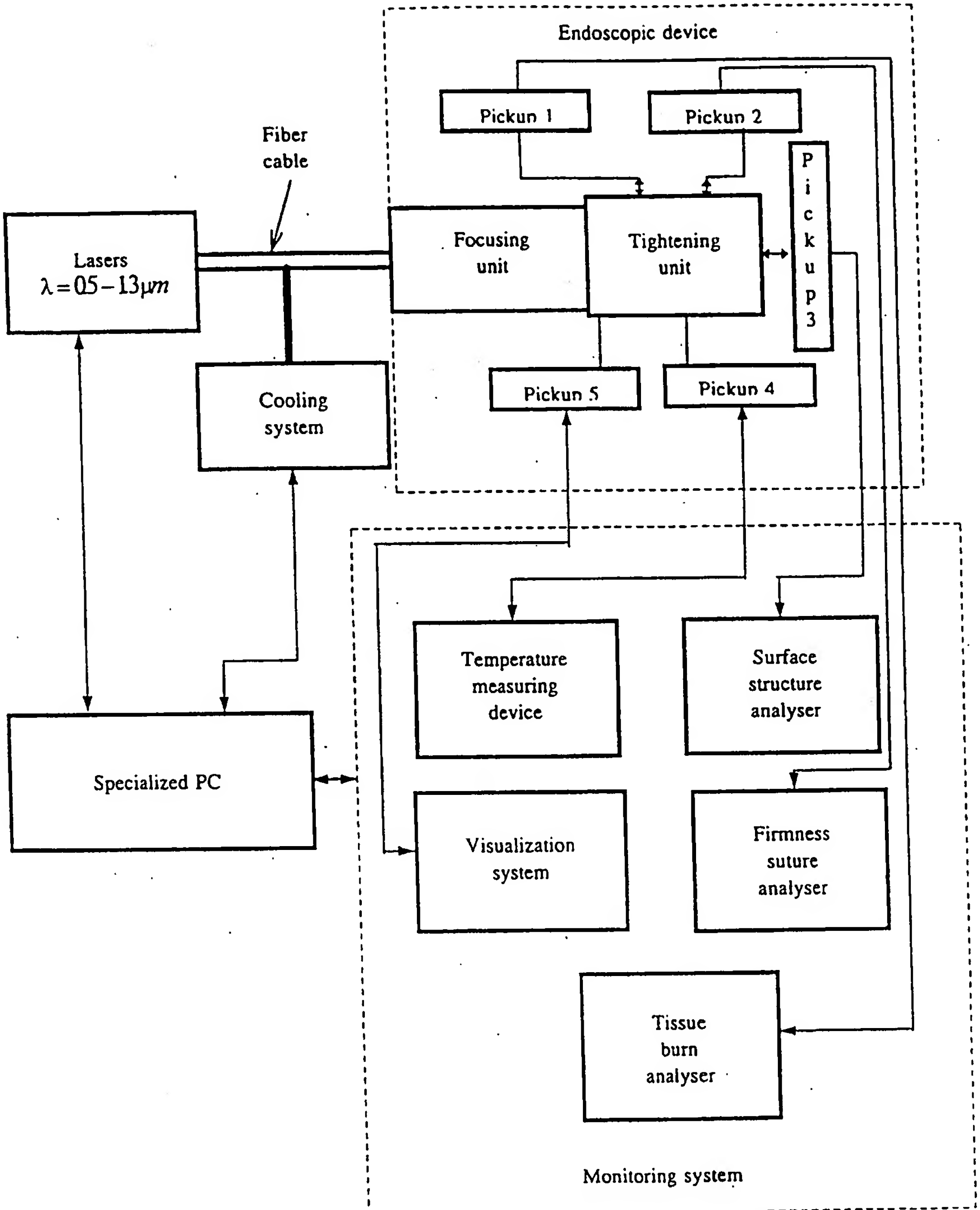

Endoscopic device
Pickun 1
Pickun 2
Pickup 3
Fiber cable
Lasers
λ=05–13μm
Focusing unit
Tightening unit
Pickun 5
Pickun 4
Cooling system
Temperature measuring device
Surface structure analyser
Specialized PC
Visualization system
Firmness suture analyser
Tissue burn analyser
Monitoring system

Figure 22

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/22726

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) :A61B 18/18
US CL :606/008
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED
Minimum documentation searched (classification system followed by classification symbols)
U.S. : 606/008

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 5,507,744 A (TAY et al.) 16 April 1996, see entire document.	1-5, 15, and 19 ----------- 6-14, 20, and 21
Y	US 5,766,167 A (EGGERS et al.) 16 June 1998, see entire document.	6-14, 20, and 21

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search
16 DECEMBER 2000

Date of mailing of the international search report
17 JAN 2001

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